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LIFE

A Study of the Means of Restoring Vital Energy and Prolonging Life

DR. SERGE VORONOFF

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LIFE

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A Study of the Means of Restoring Vital Energy and Prolonging Life

BY

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Translated by

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TRANSLATOR'S PREFACE

In this translation of my husband's *Vivre,* I have endeavored to present in English, faithfully and accurately, the profound creative thought of his scientific discoveries for restoring our vital energy and prolonging the life dear to all of us, voiced with such sincerity and eloquence in his original.

It is a book whose message is truely "universal," for it is addressed directly to every human being who lives, and wishes to live, in the true sense of the word. It describes the processes of renewal of the worn-out glandular cogs and wheels of our body in order that its mechanism shall function perfectly at a time when the brain, educated to a point where its potentialities of useful creative work are at their maximum, undergoes a decay of physical stamina threatening its powers with stagna-

tion. And this epoch-making discovery is told in a lucid, readable manner; there is no veil of technical terminology to hide its inspiring truths from the lay reader.

Dr. Voronoff, treading in the footsteps of that great Master in experimental science, Claude Bernard, makes clear that the grafting of glands will, in the future, become an every-day procedure, just as bone-grafting grew to be a common-place of surgical practice during the recent war. He shows that, as a consequence, human life may be extended to what should be its normal span of fruitful activity, a minimum age which is at present not attained. Does any scientific discovery of the ages exceed this in its importance to the individual and the race?

In presenting my husband's work in its English guise, I wish to take this opportunity, on his behalf and on my own, of thanking Mr. Barnet J. Beyer, formerly lecturer at the Sorbonne, and Mr. F. H. Martens for their splendid aid and valuable suggestions. Our thanks are also due Professor A. Elwyn, of the Col-

lege of Physicians and Surgeons, Columbia University, for his indispensable assistance and collaboration in translating Professor Retterer's *Communications* to the Paris *Société de Biologie,* on the structure and evolution of the grafted tissues.

EVELYN BOSTWICK VORONOFF.

New York, August 6, 1920.

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FOREWORD BY THE AUTHOR

DEATH shocks man with a sense of the cruellest injustice, for he treasures an intimate memory of his immortality. Every least cell entering into his composition and which, in the early days of the world's creation, formed an integral and independent being, recalls its indeterminate and eternal life, and cries out with horror at the prospect of death, which its association with other cells has imposed on it. Even now, these primitive cells, simple agglomerations of protoplasm, never die, nor do we ever find their corpses. They evolute by division; yet the two cells born of the mother-cell exactly contain her entire substance. In the course of millions of years, these cells have assembled in order to form beings increasingly complicated—from the simplest of animals, such as the amœba to such a superior creature as man—and it is this association, whose har-

mony is often troubled, which has entailed that monstrous and abnormal phenomenon, death.

In the profoundest deeps of his consciousness, or rather subconsciousness, man understands life only; since he was created for life and life alone, from his thoughts, which are immortal, to each of those cells which have guarded their recollection of creation's first intention.

This constant conflict between instinct to live and horror of dying has engendered that profound pessimism afflicting the greatest thinkers, which mingles wormwood with all our joys. It is the same instinct which in all ages has instigated passionate quests for the elixir that would allow us to extend the limits of existence to the point where the satiety of long life would finally beckon to sleep and repose.

Unfortunately, all attempts of the sort have invariably remained sterile. And this is not hard to understand. How could one find a remedy for old age when the conditions deter-

mining it were unknown? The mechanism of life has always escaped us, and we do not know the profound causes leading fatally, at certain ages, to that state of senility which ends in death. Research always has been concentrated on the affections which determine lesions incompatible with life; but the reason of our natural death has remained unknown to us. Pathological death we are acquainted with; of physiological death we are ignorant. Research in this direction has never been undertaken seriously, because of the preconceived idea that our mind is helpless as regards the discovery of nature's secret, the reason of life, and the cause of death.

This scientific dogma, put forth by the learned men of all ages, barred any investigation of this road, and no one dared sacrilege by raising the veil Nature had flung over her law of universal, objective death. Yet every dogma is an obstacle to progress, and must be cleared away in order to open the way to fructifying thought. The physical sciences have given us examples: the flight of objects heavier

than air, the transmission of the spoken word —wireless telephony—without a conductor, etc. Does biology, the science of the phenomena of life, offer us similar possibilities?

It is unquestionable that the intelligence grasps physical laws more easily than those of living nature. The analysis of the rays of a star millions of miles away from our globe, makes it possible for us to determine its composition with exactness, and to know all the metals constituting it; yet the phenomena which take place in ourselves are so complex, they offer such a tangle of physico-chemical reactions and vital manifestations—such as thought, will power—that we experience the greatest difficulty in analyzing them and in ascertaining the laws which govern them. In order to detect and discover, not the mysterious reason for life, but the actual cause of our death, we have sought to penetrate into the intimate constitution of our body, to understand the part played by the various cells composing it; and we are now able to offer the intelligent public the results of our researches.

In a succeeding work, devoted to a study of the cellular commonwealth of our body, which will be published under the title: *The Republic of the Human Body,* we shall develop this subject in all the detail it demands; but the foundation of the new conception of our life is clearly exposed in this present work, which gives the source of the means indicated to restore the energy which fails us at a certain age, and extend the limits of our lives. The experiments carried out in our laboratory allow us to hope that this goal may be attained, thanks to the graft of certain glands which pour into our organs a liquid stimulating the vitality of our tissues, and supporting their resistance against the causes of their decline. The renewal of our source of energy, when about to become exhausted, by incorporating in our organism a young gland to replace one which age has enfeebled or destroyed, would mean a solution of the agonizing problem of our precocious decline, or our death at an age when life still retains all its charms.

This book will demonstrate the solution

advanced. And it is our hope that, at the same time, the problems it presents for consideration, by awakening the interest of investigators, will call forth further new researches enriching science, and redounding to the welfare of humanity.

S. V.

New York, August 6, 1920.

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LIFE

A STUDY OF THE MEANS OF RESTORING VITAL ENERGY AND PROLONGING LIFE

CHAPTER I

The longevity of living creatures is in reverse relation to their organic perfection—The longevity of the mammals, in whose ladder of progression man stands on the topmost rung, is in direct relation to the duration of the period of growth necessary to complete bodily development—The normal life-span of man should be from 120 to 140 years—Mode or manner of life exerts but slight influence on life duration.

SCIENCE, as it is now constituted, fails to supply a single law according to which longevity may be recorded. Is it directly related to the simple organic constitution of the body? There are too few facts available with regard

to length of life among the lower animals for us to be able to make a deduction. Yet there is proof positive that among the vertebrate animals—ascending the scale from fishes to reptiles, from reptiles to birds, and from these to mammals—as organic complexity and perfection increase, length of life diminishes. Fishes and reptiles live longer than birds, and among the birds are some that reach a far greater age than do the mammals. Mention has often been made of the pike caught near Hailbronn in 1230, which lived to an age of 267 years. Carp are known to have reached the age of 150 years, tortoises two centuries, and the larger snakes and the crocodiles a period equally long. Among birds, parakeets live to be a hundred, ravens reach seventy, the wild goose eighty and the domesticated swan seventy years. Eagles are known to have lived to an age of 110 and 118 years, and falcons 160. Birds, nevertheless, never attain the great age of the crocodiles and tortoises.

The life-span continues to diminish when we rise to the mammals. Among them, leaving

man out of the question, the elephant, which would come first, may live to be a hundred; although this is not often the case. Horses rarely live fifty years; camels, forty; cattle, thirty; sheep, twelve or fourteen years, which represents extreme old age in the case of these animals.

The carnivora have an even shorter life-span. Man alone, in spite of the fact that his organism is the one most highly perfected, is able to reach an age beyond that attained by any other mammals.

Centenarians are far more common than we are accustomed to believe. In France some 150 persons aged a hundred or more die every year, and France is by no means the land most favored in this respect. During May of last year there was celebrated in Rome the centenary of Senator Count Greppi, whom I remember in 1920 as most assiduous in his attendance at the meetings of the Senate, and as seldom missing a first night at the theater. Without harking back to by-gone epochs where legend often colors truth, we may find

authentic cases of a longevity exceeding 140 years. There is the case of Kentigern, founder of Glasgow Abbey, who died at the age of 165. More authentic still is that of Drakenberg, who, born 1626, in Norway, died in 1772, at the age of 146 years. Thomas Parr, buried in Westminster Abbey, died at the age of 152 years and nine months. François Secardi Hugo, Venetian consul, died at Smyrna, aged 114 years, 10 months and 12 days. And in our own time Dr. Christaki was still living in 1896, at Constantinople, at the age of 110.

We will have occasion to cite other examples of great longevity, but can affirm without doubt that an age of 140 years is in no wise incompatible with the constitution of the human body. Incidentally, there are scientific proofs which justify the assertion. Numerous studies have been made in order to discover the laws which govern length of life. Buffon admitted that "the duration of life in its totality may, in a degree, be measured by the duration of the period of growth." Now, since the length of time necessary for any animal to

attain its normal growth is exactly fixed in each species, it is possible to calculate the age it will reach. In fact, animals are able to grow no more than a determined size, one which scarcely ever varies. They take a certain number of years, also exactly determined, in which to attain this size. Hence, longevity may be thus deduced and determined for every species. Buffon was so firmly convinced of this that he believed that "the duration of life does not depend on habit, custom, or quality of food, that nothing can change the laws of mechanism which regulate the number of our years, and that one can hardly change these save by over-eating or excessive fasting." Basing his conclusions on this principle, Buffon admitted that the duration of life was six to seven times that of the period of growth. Thus the horse, which attains his growth in four years, lives to be twenty-five or thirty; the stag, which reaches his normal growth in the course of five or six years, lives to an age of thirty-five or forty.

As for man, Buffon has calculated his lon-

gevity as from 90 to 100 years, while admitting that his period of growth ends at fourteen. In fact fourteen times six or seven would give us the figures in question. Yet as Flourens has well said, if Buffon was right in principle, in determining our longevity by multiplying our period of growth by six or seven, he was mistaken in fixing fourteen years as the terminal age of growth. The truth is that the length of time it takes our bones to grow, and the age at which this process of growth comes to an end, is twenty years. Hence, one should be able, normally, to reach an age of 120 or even 140 years, and observation has confirmed the fact. This law of stability in longevity in accord with the length of the period of growth explains why—save in a few exceptional cases—animals of large size, whose development demands more time, live longer than animals of smaller size. Mice and rabbits have a far shorter life-span than cats or dogs; sheep and goats do not live as long as the horse and camel; and these do not reach the age of the elephant. Yet, though observation agrees with

the principle established by Buffon and Flourens, which credits man with the possibility of attaining an age of 140, very few of us reach this age. Aside from a very large infant mortality, the death rate reaches its culminating point between the age of seventy and seventy-five, and yet this age can in no wise be considered the natural term of human life. In fact, the greater number of those who die in these years are still well preserved, physically and intellectually, and their death is rarely due to senile debility. The majority die as a result of infectious diseases, pneumonia, tuberculosis, or renal, cardiac or other affections, and their decease should be classed among cases of death by accident, and not as deaths due to a gradual exhaustion of vital power. Hence it would be interesting to study more closely those who have reached a very advanced age, passing the century mark, in order to see whether an analysis of their life, and their mode of existence will not disclose to us the secret of their longevity. Theoretically it would seem—and the majority of those who

have written on this question have admitted it—that a sober, moderate life, devoid of excess, offers the surest guarantee of a long existence. In support of the contention, exact observation has proved, first of all, that the majority of centenarians are poor people, the case of Sir Moses Montefiore, a millionaire who reached the age of 101 years, being altogether exceptional. Poverty being the best check gainst excess, and making a sober life compulsory, the conclusion has been arrived at that it supplies the reason for that longevity in excess of a hundred years which certain individuals have attained. Unfortunately, the problem is far less simple, and cannot be solved by a few precepts regarding a well-regulated life. The truth of the matter is that though we discover among those who have passed the century mark abstemious persons who content themselves with bread, milk, and a vegetable diet, and avoid excess in all things, we find among them many individuals who have led a wild life, who have been heavy drinkers, or have misused tobacco, coffee, and

other stimulants and drugs. Thus the surgeon Politiman, who lived from 1685 to 1825, a period of 140 years, was a heavy drinker, and from the age of twenty-five on was accustomed to intoxicate himself every night, which did not prevent him from carrying out his professional duties during the day. Catherine Raymond, who died at 107, also drank immoderately. As to the Irish landlord Brawn, who lived to be 120, he had inscribed upon his tomb "that he was never sober, and when drunk was so terrible that death itself feared him." Gascogne, a butcher of Trie, in the Hautes-Pyrénées, who died in 1767 at the age of 120, got drunk regularly twice a week.

Great smokers are also met with among the centenarians. Ross, who received a longevity prize in 1896, at the age of 104, was an inveterate smoker. The widow Lazennec, who died at 104 in Kérinou (Finistère) had smoked a pipe since her early girlhood. Among centenarians we also find some who drank coffee to excess. Thus Elizabeth Durieux, a Savoyard, who reached the age of 114, lived almost en-

tirely on coffee, drinking regularly some forty cups a day.

Are we to conclude from this that excess in the use of alcohol, tobacco, and coffee has no injurious effect? Certainly not. Their noxious effect is too well established to permit of doubt. The examples just cited, and they are numerous, merely prove that the secret of longevity is not concealed here. The manner of life we lead exerts but a slight influence, and merely predisposes us to contract or avoid certain maladies. In reality, it has no direct influence on our normal life duration. Among centenarians we even find those who were abnormally weak, such as Nicoline Marc, who died in the Boulonnais, in 1760, at the age of 110, and "whose left arm had been crippled since she was two years old; her hand being folded back under her arm like a hook. She was hunchbacked and so bent that she seemed no more than four feet in height." A sickly Scotch dwarf, Elspeth Walson, died at the age of 115.

The deduction which may be drawn from

all these facts is that the real cause of longevity must reside in some innate peculiarity of the make-up of certain of our organs which have a direct influence on the duration of our life, and which insure our existence for a longer or shorter period. This hypothesis is confirmed in addition, by the observation established that centenarians are often met with in the same family, and that in most cases longevity is hereditary. Thomas Parr, whom we have already mentioned, and who lived 152 years and 9 months, left a son who lived to be 127. Similar cases are of frequent occurrence. Yet, though longevity is transmissible, it is because of some innate peculiarity, it is due to some local cause, let us say, which parents bequeath to their children. What are these peculiarities of our constitution, what are the reasons of our more or less precocious old age, and what, finally, is the cause of our death?

CHAPTER II

Our ignorance of the origin of life no barrier to our understanding of the causes of death—The immortality of the first living being, the primitive cell—Death appeared on earth only as a consequence of the association of millions of cells to form superior, complicated beings—The specialization of the cells in our body in view of the very individual parts they play—The inability of these specialized cells to shift for themselves; their interdependence—The persistence in our organism of the primitive, non-specialized cells which have retained the characteristics of the first cells to appear on earth (the conjunctive cells and the white blood corpuscles)—The struggle between the primitive and the specialized cells—Death results when the former triumph—The victors end by invading the place occupied by the specialized cells, and, incapable of performing their duties, disorganize all their functions and arrest life—A study of various lesions established by the autopsies of all aged men, and which justify our hypothesis regarding the true cause of natural death—Experimental proof supplied by the grafting of organs—Proofs furnished by men and animals deprived of the thyroid gland.

Our study of centenarians has shown that the secret of old age is beyond hygienic pre-

scription, and that among them we often find persons who are anything but discreet and abstemious. This agonizing problem of old age is merged in that of death, and throughout the ages has haunted the minds of scholars. It has never been possible to find a solution, and as Delage, that great master, has so well pointed out: "We cannot thoroughly explain death, because we cannot thoroughly explain life." But if the initial cause of life has a purely speculative interest for us, this is not the case with regard to the cause of death. Our tremendous desire to live is in contradiction with the wretchedness of old age, and life's brevity. We possess only the instinct to live—the instinct to die is missing. That terror in the face of death, as before the specter of the physical and moral degradation of old age, which Buddha so eloquently expressed to his father, the rajah Suddhōdana, is one which all humanity shares, which all humanity suffers. Even the various religions have contributed but little by way of consolation. They have only been able to preach resignation to

the inevitable, and in order to attenuate its horror, in order to satisfy our innate craving to live, to live forever, they have promised us that we shall be reborn in another life, a life eternal. And in their immense commiseration for poor humanity, whom nothing could console for the loss of this terrestrial life, these religions have even thought it necessary to affirm that the other life will be one infinitely better.

But all in vain—atheists and believers implore God or have recourse to science in order to prolong their existence on this earth and spare themselves the degrading infirmities of old age. Unfortunately, up to the present moment science has shown itself powerless to contribute a remedy for old age, or a panacea to defer the day of death. We are acquainted with the indirect, auxiliary causes of senility, the effects of certain organic changes, the influence of certain maladies, but we are altogether unaware of the inner reason for the obligatory decline of our organs, a falling away which is bound to occur at a time ap-

proximately determined. Aside from trifling causes, the reactions of the living matter itself, of poisonings of every kind, there still remains a formidable unknown quantity. Are we able to get at it, can we penetrate the mystery of our organism and seize upon the primary cause of our old age and death? Only the solution of this problem, which will unveil nature's secret for us, could spur us on to find a possible remedy for that condition of senility of which our body offers so lamentable a spectacle at a given age. Arduous though it be, this problem should not be regarded as above or beyond the limits of scientific investigation.

The impossibility of sounding the origin of life, and the appearance on earth of the first living being, should not exclude the understanding of what causes death. In fact, the origin of our life harks back some millions of years, and it is impossible for us to actually reconstruct its atmospheric conditions: heat, humidity, composition of the air, and the exact specific state of matter at the moment, which

made possible the birth of life. Death, on the contrary, is a phenomenon which takes place before our eyes, and which we have only too frequent an opportunity of observing.

Our study might extend from the simplest being to the most complicated of organisms. We may even verify by experiment a hypothesis which observation has suggested to us; for, though it be impossible for us to create life artificially, yet we may artificially alter its modal character, provoke precocious senility, and bring about the conditions which hasten or retard death. Research in this direction, therefore, is permissible, and the non-success of previous efforts should not discourage any renewed attempt to solve this most serious, most passionately vital problem for humanity.

And first of all the question arises: Is death inevitable, does it present itself as a universal law which no living creature on earth may escape? I am speaking, be it understood, of natural death, physiological death, not of death provoked by accident, illness or the aggression of the strongest—all causes which we

are habitually permitted to observe in nature. I do not know that this natural, physiological death has ever been observed in the case of man, for even men who die at an extreme old age, without any apparent illness, when an autopsy is performed, show lesions and alteration of tissue which had escaped observation, and which offer decisive proof that death had been caused by more or less serious lesion of certain organs.

Hence, if natural death does exist—and it is impossible to deny it—it should not be of frequent occurrence at the age when it usually takes place. On the other hand, in order to study this phenomenon, in order to surprise nature's original intention, it is logical to have recourse to the most simple of all beings, the one nearest that which first made its appearance on earth. Only in this way can we decide whether death was established at the beginning of life, and whether it is an unavoidable law of nature. Now, the most elementary form of living matter presents itself to us in the shape of a cell composed solely of a small,

soft mass, the protoplasm, containing, in its interior, a nucleus. Such are the infusoria, the amœbæ, and the other protozoans (Fig. 1). In observing them, one will soon see that each of them divides itself, constituting two living cells, without the least particle of matter perishing. Each of these two cells again divide into two parts and "one may observe them reproducing by means of division, and swarming about in the most extraordinary fashion in a short space of time. Generations succeed each other with great rapidity, without the occurrence of a single death; one vainly looks for one corpse among the innumerable multitude of swarming infusoria." (Metchnikoff). They would be capable of overrunning the whole world, were it not that being defenceless creatures, they are devoured by innumerable enemies. When, after a long succession of divisions, a certain exhaustion is noticeable in the infusoria, as a consequence of the impoverishment of their nutritive ambient, instead of terminating their existence by death, they may join themselves together by drawing near each

other, two by two, and emerging from this fusion rejuvenated and full of activity, recontinue their series of divisions. The amœba never dies. It may be destroyed by an enemy or as a consequence of inanition due to lack of

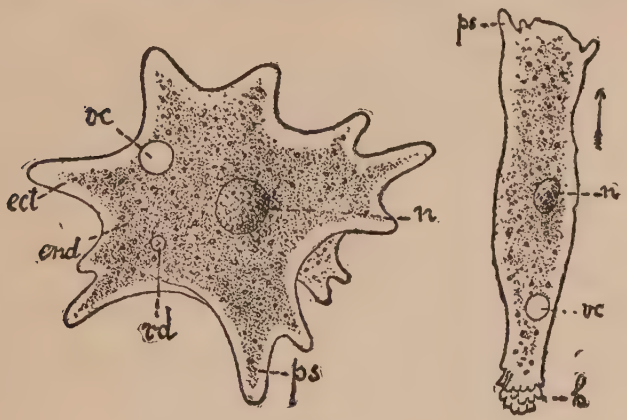

FIG. 1

To the left. Amœba. A schematized figure. *End*, endoplasm; *ect*, ectoplasm; *ps*, pseudopods; *n*, nucleus; *ve*, contractile vesicle; *vc*, digestive vacuole.

To the right. Protean amœba in movement, after nature (Demel). The arrow indicates the direction of movement. *ps*, anterior pseudopods; *h*, posterior prolongation; *n*, nucleus; *ve*, contractile vesicle (After Emile Yung).

food, but physiological death is unknown to it. In creating the first living creatures, from which, in gradual succession through millions of years, the animal chain has developed, na-

ture wished them to live forever. The breath of life which for the first time gave animation to matter held nothing but life. Nature at that time knew nothing of death. What then are the circumstances which led to the fatal changes in this initial plan?

In order to understand it, we must follow the progression which has taken place in the constitution of living beings. The individualities of the first order, formed of a single cell, completely endowed with life, are succeeded by organisms made up of a grouping of several simple cells. These last are followed by beings more and more differentiated, complicated, gifted with organs destined to accomplish a special function, and hence composed of cells far removed from the primitive type. Each of them, in fact, has had to acquire individual qualities which enable it to play a useful part in the group. The appearance of these different cells which enter into the constitution of our body is so different from that of the type-cell, of the primitive protozoan first to appear on earth, that it is difficult to recognize in them

the elements of the initial cell. Nevertheless, the study of the cell, as one ascends the degrees of the ladder of being, shows us every step of the transition, and one is able to realize at once how the muscle-fibers, the nerve-cells, etc., developed (Fig. 2). But no matter how complicated, how perfected a creature—even man—may be, it always harks back to a single cell—the ovule, or the egg. The transformation is produced in proportion as this initial cell splits, and divides more and more frequently, in order to form, little by little, the different cells which again enter into the composition of our tissues and organs. These cells, very greatly modified, incapable of carrying on an independent existence, and continuing to be self-sufficient, are only assured of life by the mutual concurrence of all the cells of the body. They form a society, a state, in which each plays a special part destined to ensure the collective life. The higher, the more delicate the function of each organ, the more perfected the cells of which it is composed, the more these cells depart from the primitive type, and the

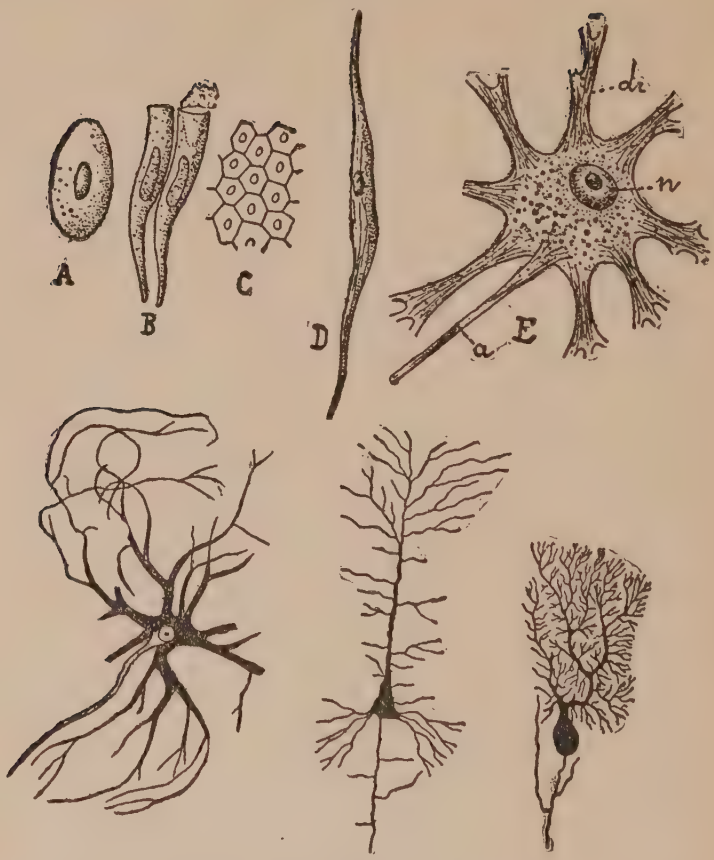

FIG. 2.—VARIOUS CELLULAR FORMS

A. Red corpuscles of the grasshopper.

B. Epithelial cells of the intestines of the fish.

C. Cells of the epidermis of the grasshopper.

D. Muscle-cell of the riband-muscle of a snail (After Prénant, Bouin and Maillart's *Traité d'Histologie*).

E. Nerve-cell of the human spinal marrow; *n*, necleus; *dr*, dentrites; *a*, exone.

Below, some types of the nerve-cells of the human marrow, cerebrum and cerebellum (After Deiters).

more they find themselves dependent upon the labor of the cells belonging to other, less perfected organs.

The primordial faculty of the cell, which is to be sufficient unto itself, and to reproduce, is lost in increasing measure. It even disappears completely in the case of the nerve-cells, which are the noblest, the most perfected factors of the organism. Once developed, during embryonic life, they remain so for their entire period of existence, without regenerating or multiplying. Having acquired the loftiest properties, and specializing in psychic functions, they have completely lost the qualities which characterize the immortal primitive cells, that is to say the faculty of reproduction.

Just as in the social world of humanity, a process of selection takes place in the human organism, a hierachy among the various elements composing it, from the humble intestinal cell which, so to say, prepares our daily bread, to the delicate and highly perfected cerebral cells which coordinate the labors of all our organic artisans, stimulating some, moder-

ating others, and forming a kind of Roman senate for our cellular republic.

Yet by the side of all these more or less perfected, specialized cells, by the side of all these laborious citizens, each of whom is exercising some particular trade, we find primitive beings, incapable of performing any function calling for a professional education. These cells, but slightly differentiated, are an approach to the primitive type, the ancestor whose life was reduced to capturing food and reproducing himself—they are the *conjunctive cells* (Fig. 3), and the *white blood corpuscles* (*leucocytes*) (Fig. 4). The former have everywhere infiltrated themselves. They are found in larger or smaller numbers among the elements of all the organs, without exception. The latter float freely in the blood; and are able to pass through the slight walls of the capillary vessels into all the tissues. These *conjunctive cells* and the white corpuscles are the proletariat, a robust race, reproducing with great facility. A close relationship unites these two elements, and there are numerous

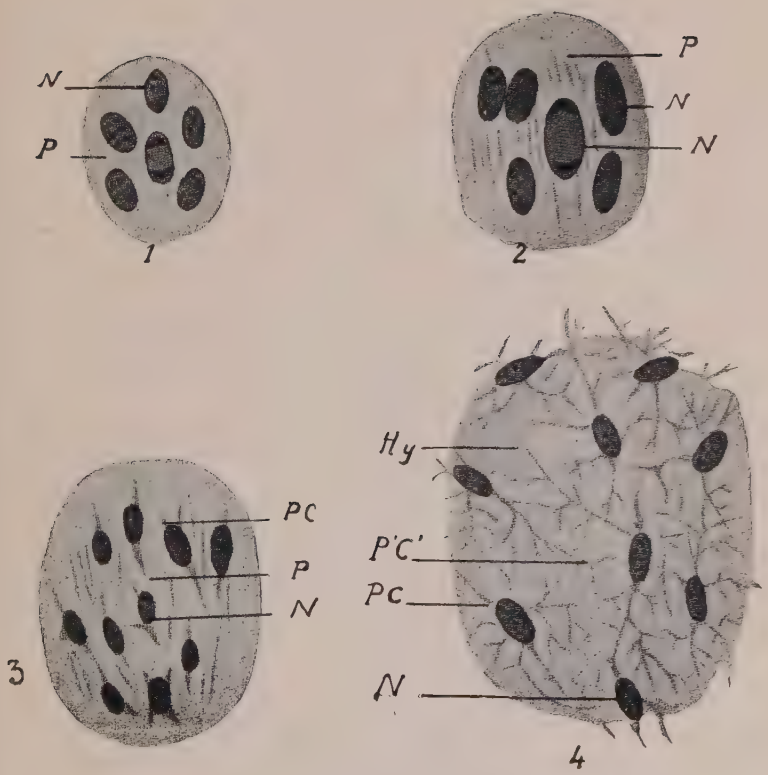

FIG. 3.—CONJUNCTIVE CELLS

1 and 2. Conjunctive primordial tissue.

3 and 4. Two stages of its transformation into reticulate conjunctive tissue.

N, nucleus; *N'*, nucleus in mitosis; *P*, protoplasm; *PC*, chromophile protoplasm; *Hy*, hyaloplasm (After A. Branca's ***Précis d'Histologie***).

circumstances under which the white corpuscles change into *conjunctive cells.*

Sturdier than all the other cells, they wage within us, from the hour of birth, a relentless struggle which knows no truce, against the nobler cells of our body. These succumb in the

FIG. 4

White blood corpuscles. *L*, Large lymphatic blood corpuscle; *l*, small lymphatic corpuscle; *p*, lymphatic granular cells; *v*, *v*, *v*, *v*, a similar lymphatic cell, reproduced at two-minute intervals, in order to show its changes of form, analogous to those of an amœba.

long run, victims of the sacrifice they had made of their independence in order to take over a limited rôle, a special function, which aided the entire community to prosper, but did so at the expense of their own individual powers of resistance.

Like any highly organized society, where the division of work is carried to its most extreme limits, our bodies discover that they are at the mercy of primitive elements which tend to level society, and bring it back by original instinct to the first state where each cell was sufficient unto itself. But our organism, where all is coordinated, is fated to succumb to this leveling process.

The study of old age teaches us, in fact, that the conjunctive cells invade the tissues or our organs in an ever increasing degree. The autopsies of aged men invariably disclose the disappearance and atrophy of the differentiate, specialized cells, which are replaced by *conjunctive cells,* which leads to sclerosis of the tissues. And, in proportion as the number of cerebral cells diminish, the *conjunctive cells* replacing them are in no wise able to carry out the functions of those which have disappeared. Our cerebral faculties grow increasingly lower, the coordinating influence of the brain on the organs weakens, and when the number of cerebral cells no longer suffices, when our

brain contains too great a number of these *conjunctive cells,* incapable of ensuring the functional harmony of all the organs, then death strikes our body deprived of guidance. But the brain is not the only organ attacked. We have already mentioned it as being the most important, the most perfected organ of our organism. The same phenomenon may be observed in all the other tissues. Everywhere we can verify the atrophy of the original element and the substitution of conjunctive tissue in its place. Even the bones undergo the common fate. Primitive cells (the osteoclasts) multiply around the osseus laminæ, whence they draw the pith of the bony substance; wherefore we have those fractures of such frequent occurrence in the case of old men.

Part of the lime thus liberated passes into the circulation and is deposited along the walls of the arteries, already changed by the invasion of the *conjunctive cells,* makes them hard and brittle, robs them of their elasticity, and renders them unfit for nourishing our organs.

These are the most characteristic lesions of

old age, known under the name of arteriosclerosis. The muscles, in their turn, experience the invasion of the primitive protoplasm (the sarcoplasm), which destroys the contractile substance. The muscular fibers grow smaller, hence the muscular weakness which shows itself well in advance of the decrease of intellectual activity. Beginning with the age of sixty, muscular effort grows painful, atrophy having taken possession of too large a muscular surface. In the liver, those cells which play the most important part are also those replaced by *conjunctive cells.* The same phenomenon takes place in the kidneys, where the *conjunctive cells* end by obstructing the tubes meant to relieve the organism of waste. Everywhere, in the tissues and organs, it is the *conjunctive cell,* which, first holding a modest place, multiplies, and strangles and atrophies the nobler cells, usurping their place and, incapable of fulfilling their duties, introduce a species of anarchy into an organized society and cause its death.

This phenomenon may be experimentally observed in the grafting of organs. The grafted organ, for a certain space of time, before the formation of new vessels, is deprived of blood nourishment. A certain number of cells, unable to endure this prolonged fast, atrophy, disappear and a part of the organ ages prematurely. Now, which are the cells which suffer this atrophy? They are the nobler cells, the most differentiate cells, adapted to play some special part in the organ in question. And which are the resistant cells which, later, when supplementary circulation has been established, invade every opening left by the disappearance of the nobler cells? They are the *conjunctive cells,* which invariably possess this primitive element, resistant, little differentiated, strong like their ancestor whose principal quality they retain—their great power of multiplying themselves, of returning even to their simplest embryonic state. Hence this phenomenon is general and, aside from all trifling pathological conditions, it is the key to the mystery, the reason why we age,

and the cause of our death. Nature tends to bring us back to the primitive type, the simple cell; but our perfected organism, in which all the organs depend upon one other, where the weakening of one reacts on all the rest, is no longer able to undergo this simplification, and the brutal element which overruns it destroys its functional harmony, brings about our death, and perishes with us.

Another proof, one indirect but very enlightening, with regard to the intimate process of aging, and this struggle between the simple element represented by the *conjunctive cell* and the nobler specialized elements of our body, is furnished by the patients attacked by cretinism (Myxœdema), an affection easy to reproduce experimentally in animals by removing their thyroid gland (Fig. 5). One knows the mask of old age worn by individuals thus afflicted. Even though they be children they seem more like prococious old men; with wrinkled face, dry and spongy skin, a low temperature, sparse hair rapidly turning white, great muscular weakness, a tendency toward

FIG. 5

Young pigs from the same litter, born April 28, 1892, raised under identical conditions. Photograph, July 10, 1892.

To the left, normal subject; *to the right*, subject thyroidectomized May 13, 1892. (After G. Moussu.)

sclerosis, especially vascular sclerosis, an arrested state of bodily development, sadness, and apathy.

Anatomically, these lesions are quite accurately shown by hypertrophy of conjunctive tissue, which leads to premature senility. Now what is the rôle in our organism of the internal secretion of the thyroid gland, whose absence gives rise to these phenomena? All physiologists are agreed that its action consists in augmenting the excitability of the nerve-cell, but above all, *in moderating the activity of the conjunctive tissue.* The thyroid secretion regulates and moderates the life of the conjunctive tissue, restrains its activity and serves, so to speak, as a check on the invading tendencies of these primitive members of the cellular republic of our body.

The absence of the thyroid gland, in depriving the body of this guardian of the activity of the conjunctive tissue, allows the latter to develop in an excessive degree. The cells divide and multiply with extraordinary activity, atrophying and suffocating the nobler ele-

ments among which they find themselves, taking their place, and, in the course of a few months, accomplishing the evil work which as a rule it takes them years to complete. The thyroid gland pours no elixir of youth into our veins, but it does fight against the encroachment of the robust, primitive, non-specialized cell, and prevents it from taking the place of those trained to play a special part in our body, for it is this encroachment which destroys the harmony of the organism, troubles and weakens its functioning, brings on old age and hastens death.

The initial cause of old age having thus been elucidated, it is certain that the secondary causes which may accelerate the state of senility and abridge our existence are numerous. Metchnikoff is right in dwelling upon the harmful effects of the fermentation due to the bacilli of the large intestine. The poisons there elaborated, reabsorbed by the blood, quite naturally change the most delicate, precious and sensitive elements of our body, and those which are least hardy. On the contrary, the

conjunctive tissue formed by simple cells is infinitely less influenced by these toxic products, and while the former atrophy and perish, the latter invade the territory opened, and disorganize the functions devolving upon the atrophied cells. The same observation might be made with regard to alcoholism, aggravated by the fact that this poison (a product of yeast fermentation) even seems to superexcite the activity of the *conjunctive cells,* whence rapid sclerosis of the vessels and organs in general develops. But we will not enter into this subject, which belongs to medicine in general. What we have essayed to do, has been to establish the fundamental *processus* of all old age which leads to our death: the struggle of the *conjunctive cells* of any and every origin, the simple cells, against the highly differentiated cells, a struggle which ends in the triumph of the former, a triumph of anarchy, the ephemeral reign of the elements of brutality, whence proceeds the disorganization of all functions, and the ultimate death of the organism.

CHAPTER III

Why the primitive cells persist in our organism—Older theories anent the mechanism of life, supposed to result from a first impulsion given at birth—The new conception which explains the mechanism of life by the impulsions, continually renewed, which the organs receive from certain enclosed (endochondral) glands—The relation between the functioning of our organs and the internal secretions of the glands: thyroid, pituitary, suprarenal, etc.—Identity of the secretions of human and animal glands—Effects of this secretion in connection with the greater or lesser perfection of the organs on which it acts.

Since old age is the triumph of the primitive over the differentiate element, can we intervene in the struggle in order at least to defer the date of this fatal victory? Presumptively, one might hope to do so, since victory is often our portion even in the trenchant conflicts between life and death following infectious maladies. Unfortunately, the situation

is far from being the same in both cases. In a malady we have to do with a foreign enemy, a microbe coming from without, and our means of action may tend to destroy this intruder, whose death is the ransom of our own life. The struggle between the two elements which, both of them, form an integral part of our own organism, has quite a different aspect. What further aggravates the situation is the fact that the *conjunctive cell* does not injure us until it ceases to play its part, and endeavors to trespass on the territory legitimately occupied by other members of the same social body. Originally it appears in the constitution of our body as a useful element with which we could not dispense. It is, in fact, the conjunctive tissue which forms the substratum, the supporting mass for the remaining tissues. The blood-vessels, the nerves, the muscular fibers, as well as the cells of all the other organs are supported by the conjunctive tissues, which form a species of solid framework, necessary to uphold the edifice.

On the other hand, the *white corpuscles* in

our blood, the source of the continual formation of new *conjunctive cells,* the reserve which increases their number, are actually our principal defenders in the struggle against alien enemies. Robust and very mobile, always ready to devour indiscriminately all that they find in their way, their enfeebled friends on the inside as well as their enemies from without, they do not spare the microbes and thus render valuable service to the specialized cells of our body, too perfected, too delicate themselves to support such a struggle with any hope of success. Hence, we cannot search for some means to destroy them as we do in the case of the harmful agents that come from without. Our intervention, where they are concerned, can only consist in moderating their tendency to multiply too rapidly. Yet, though we must be very circumspect as regards our action against these burdensome and prolific neighbors of our nobler cells, it seems logical, for that very reason, to concentrate all our efforts in reinforcing these last, in stiffening their resistance against the invasion of the

conjunctive cells, in coming to their aid in this struggle whose stake is our youth, our energy, our equilibrium, and the harmony of all our functions. Have we the means of so doing? In all ages men have tried to rejuvenate organisms which had aged. Without mentioning the alchemists, and all those more or less fantastic attempts made during the Middle Ages to discover the elixir of longevity, minds as serious as those of Descartes and Bacon passionately followed this quest. In our own time the illustrious biologist and philosopher, Metchnikoff, thought he had discovered the remedy for our old age in warring against the injurious microbes of the large intestine by means of lacteal alimentation, especially curds, and yogourt. In fact, these last contain large non-injurious bacilli which fight against our evil little intestinal microbes. Yet this remedy, like so many others, belongs to the arsenal comprising all hygienic measures worth following. It is in no sense a panacea for our old age, whose deep-seated causes we have just considered. Which then would be

the really efficacious means of combating these first causes established at the beginning of our life? In order to answer this question we must penetrate into the intimate mechanism of our tissues, and account to ourselves for all that conditions their life and functions. In so doing we enter a field shrouded in mystery only some eighty years ago. In spite of the fact that the study of the human body harks back for centuries, these essential wheels were unknown to us. It was well known that every organ played its part from birth; that the psychic functions devolved upon the brain; that the heart pumped the blood through our arteries, contracting every second without pause for some eighty or ninety years; that our alimentary canal elaborated the nutritive matter of which our system stood in need; that the kidneys served as a drain to cast out organic waste matter, etc.: but no one thought to ask by what miracle each of these organs fulfilled its functions without pause or rest, our whole life long.

Everyone, according to his religious convic-

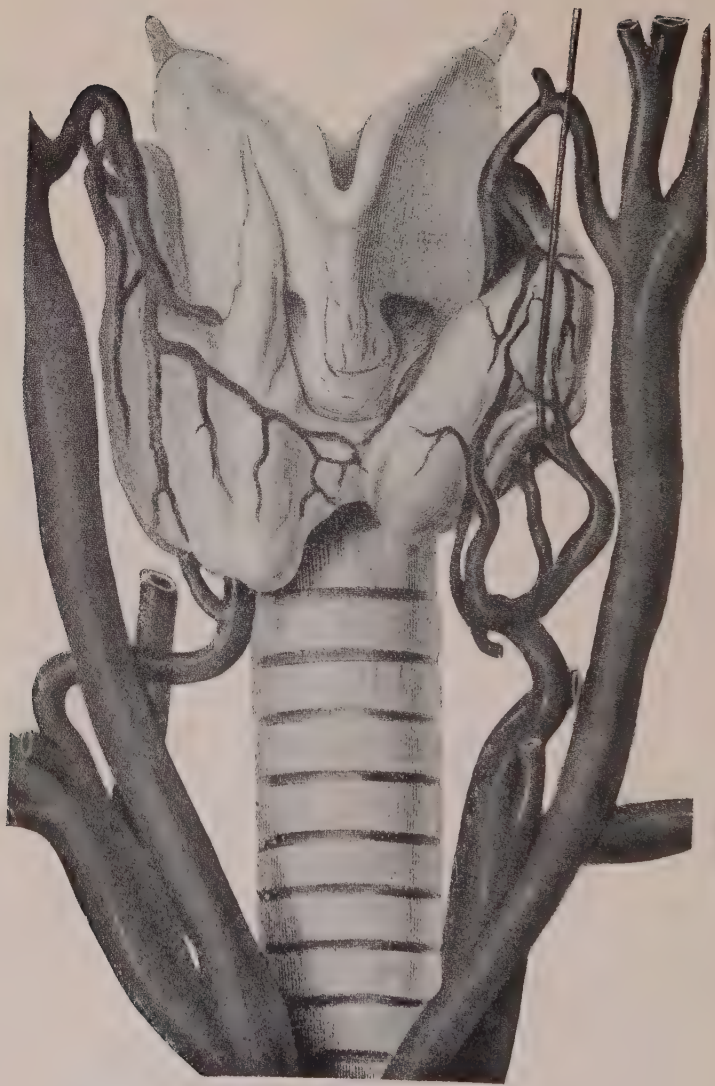

FIG. 6.—THYROID GLAND OF AN ADULT MAN

The gland is shown resting against the cartilages of the trachea and, on either side, the caratoid arteries and the arteries of the thyroid gland (After O. Tillaux. *Traité d'Anatomie topographique*).

tions or his philosophical ideas, sought the reason for this continuity of function either in the will of the Creator, who has instilled in us the principle of life, or in a sort of general initial impulse which nature generously presents to each of its creatures. And then—a rude awakening to a disconcerting fact, thanks to the methods of experiment whose value has been emphasized by Claude Bernard in particular: It developed that it was only necessary to remove a man's thyroid gland (Fig. 6), a gland situated in the middle of the neck, quite a distance from the brain, in order to cause him to lose his psychic faculties, and become incapable of formulating a single thought. At the same time it was noticed that the development of the body ceased (Fig. 7), that the skin grew thick and dry, that the hair fell out, that the tissues were overrun with fat, and that the conjunctive cells, as if liberated from restraint, invaded the organs and transformed a youthful being into a precociously old man. Thus all our organs, even the most noble among them, the one which in our pride al-

lowed us to compare ourselves to God, by reason of the power of our thought, all these organs depended on a liquid which the thyroid gland elaborated and continually poured into our blood, charged to carry it to all our tissues to ensure their functioning.

Still worse is the result of the removal of the four small parathyroid glands, no larger than pinheads, situated at the side of the thyroid gland. All our nerve-cells at once abandon themselves to the maddest over-excitation, communicating the most violent contractions to our muscles, and causing death in terrible convulsions within a few days' time. The nervous system, deprived of the secretion of the parathyroids, loses all control of its actions—all balance in its functions. It no longer knows what it is doing, so to speak, and instead of imparting the regular contractions adequate to the demand, it provokes inordinate movement, disjoints the actions of all our muscles, and causes our death. Hence these small glands are marvelous workshops in which is prepared a liquid destined to mod-

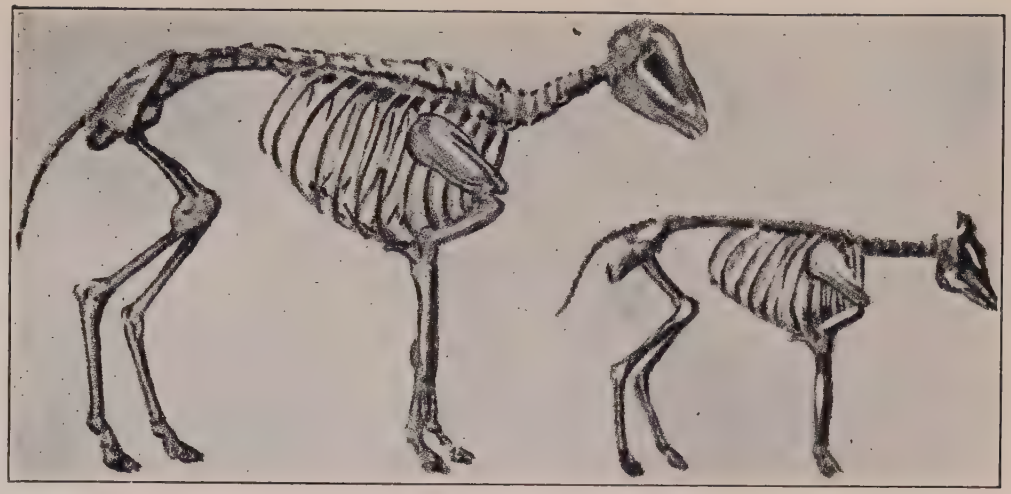

FIG. 7

Arrested development of the skeleton after the ablation of the thyroid gland (A. von Eiselberg). Skeleton of a sheep eight months old, thyroidectomized eight days after birth, and of a test sheep of the same age.

FIG. 8.

The Right Kidney. 5, suprarenal gland (or capsule) capping the upper extremity of the kidney (After Testut and Jacob, *Anatomie topographique*).

erate and regulate the activity of our nerve-cells, and proportion their efforts to useful needs. And other glands play a part in our bodies no less important. When the suprarenal glands, these two small glands each of them situated above the kidneys are removed, death infallibly ensues at the end of about thirty hours (Fig. 8). Extreme muscular weakness results, the heart beats more and more slowly, and the animal on which this operation has been practiced dies with every sign of extreme exhaustion like men attacked by Addison's disease, due to the gradual destruction of these glands. Our heart, therefore, during the entire course of our existence, does not contract thanks to a first impulsion supposed to be given by nature at the birth of a living being. A liquid secreted by the suprarenal glands is necessary to lend constant support to the beat of the heart and the contraction of the arteries.

No less important is the rôle of the gland known as the pituitary (hypophysis) gland, a small gland found beneath the brain, on a level

with the palate of the mouth. It is no longer than a hazelnut, it weighs little more than half a gram. And yet its complete removal is followed by death in forty-eight hours, or in five days at the most. After the destruction of this gland the animal grows somnolent, its respiration becomes slower, its temperature drops, and it dies in a state of coma.

The effect of hypertrophy and of partial atrophy of this gland on man has been observed. It is a most curious one, and proves how largely the functioning of all our organs is conditioned by the secretions of various glands, the most essential machinery of our body. Despite its small size the pituitary body is subdivided into two lobes, each of them presiding over a special function. Hypertrophy of the *anterior* lobe, in a child, before the growth of the bones has come to an end, allows these bones to reach an exaggerated length; the person in question grows to a gigantic height (acromegalia); his hands and feet attain an enormous size; his jaws take on unusual proportions; his muscular development becomes

FIG. 9

Effect of the destruction of the *posterior* lobe of the pituitary gland (Cushing).

To the left is shown a dog that has undergone this operation. The tendency to adiposity is well marked.

To the right a test dog of the same age (After A. Shaefer).

considerable, and the subject gives evidence of extraordinary strength (Fig. 10). When, on the contrary, the secretions of this *anterior* lobe are insufficient, the body remains short, hands and feet stay small, and the skin is soft and delicate (Fig. 11). The secretions of the *posterior* lobe has no such effects. It stimulates the lacteal and renal secretions, influences the development of fat, and also stimulates the contraction of our visceral muscles (Fig. 9).

There are other glands whose function is still shrouded in mystery, such as the pineal gland, which is found in the middle of the brain (on the roof of the dorsal wall of the third ventricle) where the ancients placed the seat of the soul. In some reptiles a medial eye is developed on the level of this gland. All that is known for the moment concerning its function is its influence on the development of the sexual organs; but new studies are needed to make its rôle clear. We intentionally put aside, for the time being, a consideration of the sex gland (testicle), whose description calls for more complete development.

But what is important to remember in this review we have just passed of the rôle of the glands in our organism, is that life, that the functioning of all our organs depends on them, and that they determine the action of each. The brain, the nerves, the muscles, as well as the liver, the kidneys and all the other organs, would be incapable of playing any useful part without the aid of the glands. The suppression of the stomach, of a large portion of our intestines, of a kidney, is infinitely less prejudicial than the suppression of the minute parathyroid glands, the suprarenal glands, etc. The functioning of our organs is no more than the result of the activity of our glands, and when the bodily functioning is disturbed, the cause, in most cases, should be sought, not in the condition of the organ itself, but in the condition of the gland which controls it. And, marvelous to relate, these glands perform the same functions in all animals, secrete the same liquid, produce the same effect as in the case of man. The internal secretion of the gland of a sheep or a dog is identical with that of

FIG. 10

Effect of hypertrophy of the *anterior* lobe of the pituitary gland (hypophysis). The giant Hugh, aged 25, height 7 11/20 feet (After Launois and Roy).

Fig. 11

Effect of insufficient internal secretion of the *anterior* lobe of the pituitary gland. To the right C. H., aged 51 years. To the left, his brother, aged 32 years (After Evans).

(Stephen Chauvet. *Infantilisme hypophysaire.*)

a man, and if one could transplant their glands into a human being, one would secure the same influence on the functioning of the organs it controls as was exercised by his own gland. And this would be quite as true in inverse measure. If one could graft the gland of a man on any animal the gland in question would act like that of the animal. The reason is that all these glands act solely through the chemical substance they elaborate, and that this substance is always the same. That which differs is the quality of the tissues which receive this identical liquid, their degree of perfection, their evolution in the animal scale. The thyroid gland of a man acting upon a dog's brain could only rouse the animal in question to action in harmony with its own nature, its canine capacity for manifesting thought and feeling. On the other hand, the thyroid gland of the same dog, in pouring into a human organism the chemical substance which every brain requires in order to perform its functions, will translate these functions in accordance with the capacity of the cerebral cells,

which have reached a degree of perfection which those of the animals have not attained.

All opotherapy is founded on this fact, and we have recourse to the glands of sheep, calves, etc., in order to make good insufficiencies in the functioning of human glands.

If I may allow myself a comparison, I might liken the action of the glands to that of the electric spark of a magneto which moment by moment lights the gas and produces the explosion in the cylinders of an auto-motor. The spark is always the same, for a ten or a hundred horse-power motor; but the effect differs and corresponds to the amount of power which each of these motors is capable of generating.

As the mind is convinced of these truths, medicine will undergo a gradual process of evolution in the direction of glandular therapeutics. Aside from microbial infection, the functional troubles of our organs being nothing else but the result of a glandular secretion, we will concentrate upon the cause, and not on the secondary harmful effect betrayed by the organ affected. By means of a thorough

knowledge of the effect of each gland, of the territory it controls, the functions which depend upon it, we shall be able to penetrate the consummate mechanism of our organism, and may often be able to master it. These glands, so small, so mysterious, so profoundly imbedded in our tissues, avoiding our investigations, have remained unknown for centuries, and for centuries we have known nothing of the essential machinery of our own body. One might think that Nature had wanted to hide her secret from us, and it is only painfully, after age-long efforts, that we have succeeded in wresting it from her. How many maladies in which the effect of injurious bacilli could not be pointed out, have remained unknown to us owing to our ignorance of the part played by these glands, and what a marvelous source they offer us for establishing the balance of the functions of our organs. Across the millions of years Nature has groped, sought, suppressed the organisms which were valueless, and little by little formed beings whose organs are admirably coordinated to in-

sure a perfect functioning of the body, adapted to conditions of life on this earth of ours. In the case of a being normally constituted, if this functioning is subjected to a disturbance, if our heart gives way, if our muscles grow feeble, it is because the gland which controls them has been disturbed, or has undergone a change. To manage these glands at our convenience, insure their vitality, the continuity of their action, stimulating the one, replacing the others, is to make ourselves masters, so to speak, of our own bodies.

CHAPTER IV

Senility as the result of the gradual destruction of our specialized cells by primitive cells to be corrected by increasing the vital energy of the specialized cells—The sex gland as offering a marvelous source of such energy—The effect produced by its removal—A study of the eunuch—A study of the old men whose sex gland continues to function, and of those in whom the gland has atrophied—Studies of men of genius in connection with the functioning of the sex gland.

We have formulated the ideal toward whose realization our efforts should be directed, yet a fatality weighs upon us: it is the intestinal strife, deeply seated within our tissues, the battle which the primitive cell, the *conjunctive cell,* is continually waging against higher specialized elements of our organs, and which stamps them with the stigma of age and decline wherever it triumphs. Those cells which are finished, perfected, and specialized in the

highest degree for a particular function, those whose labors are most intense, are the first to weaken, yielding their place to the robust invaders, and eventually succumbing.

Now stop to reflect on the high degree of perfection which the cells of our glands, our glandular cells, must attain! They are often no larger in size than a nut and there are some of even smaller dimensions. Hence, in the nature of things they contain only a very limited number of cells to do an unthinkable amount of work. In the majority of cases they even divide this labor among themselves, forming separate "gangs," each charged with the task of producing some different fluid to act upon this organ or that.

The thyroid gland, whose principal function consists in moderating and slowing up the activity of conjunctive cells, also allows itself to be invaded in the long run by its prolific neighbor; the number of its cells charged with elaborating the precious liquid diminishes, and their moderating influence, weakening as they disappear, leaves the field open in increasing

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measure for the continually growing activity of the conjunctive cell. Our health, the conservation of our youth and our activity, the harmonious equilibrium of all our functions cannot be preserved, therefore, unless we find ways and means of aiding our specialized organic cells, those in particular which have assumed the most important and essential functions—those of our glands of internal secretion. Hence we cannot repeat too often that to give all these cells greater vigor, to support their vital energy so that they themselves may resist the pressure and invasion of the conjunctive cells for a longer period of time, must present the most logical solution of the bitter problem of our decline and aging.

Fortunately Nature, which created us that we might live, and endowed us with a powerful mechanism for the movement of our organs, has at the same time provided us with a marvelous source of energy. It is a gland which has been selected to furnish this energy, for it is invariably the glands which are charged with the task of elaborating the prod-

uct capable of influencing various organs or even the whole organism, at a distance.

Such, in fact, is the part played by the testicle, the distributor of energy, which stimulates the immense bee-hive known as our body, where the sixty trillions of cells composing it labor ceaselessly, each carrying out some function definitely fixed.

What then are the internal secretive properties of this gland? In order to understand them we need only deprive the male of the gland and observe the effect of this privation upon his organism.

Castration, therefore, makes it possible for us to study the rôle of the sex gland. And since it is much used in the case of domestic animals, and in the Orient, with regard to man himself, we have at our disposal a large field of observation. It seems preferable to begin our study at once with the consideration of castrated human beings (eunuchs), not alone because we have had opportunities of observing them in the course of several years spent in Egypt; but also because they are castrated

when very young, before the age of puberty, and before the body is fully developed. Hence their organism is entirely deprived of its internal secretion, which makes it possible for us to determine the real effect of this secretion in an exact manner. Animals, on the other hand, are usually castrated at an age when their bodily development has nearly come to an end, which allows the animals in question to retain certain qualities already acquired under the influence of the sex gland, which had been able to function for a certain length of time. Again, the study of man offers the further advantage of allowing us to estimate the modifications to which the intellectual and moral faculties have been subjected, which are difficult to determine in the case of animals.

Castrated at the age of six or seven years, these eunuchs, when adults, have a certain marked appearance which at once sets them apart. As a rule, they are tall, because of the abnormal length of their tibias, their faces are glabrous and livid, and their hanging cheeks

make them look like old women. Most of them are fat, with rounded outlines and, in many cases, voluminous breasts. Their flesh is flabby and their muscular development curtailed. Their voice is infantile, in consequence of the arrested development of the larynx, and often discordant. Their bodily vigor being much diminished, they are incapable of doing work which calls for any extended effort. Their blood is poor, and anemia accentuates their weakness. In short, a physical decline seems to have stricken every organ, and one is confronted with fallen, languishing creatures, whose vitality has been sapped in every respect. Their intellectual and moral falling away is no less marked. All labor being hard for them, they are naturally lazy, indolent and without energy. Their faculties of affection are largely effaced, and egotism is not the least of their defects. As timid as capons, they readily sacrifice their self-respect, incapable of an energetic answering thrust. They age prematurely. At thirty or thirty-five, their skin loses its suppleness and grows spongy.

After forty, the circle of senility of the cornea is permanent. They rarely live to an advanced age. Their intelligence is greatly weakened, and the few eunuchs who are cited as playing a notable rôle in ancient Byzantium were castrated when adult, and thus were able to retain, at least in part, qualities they had already acquired. Even under such conditions the vitality of the organism, not being supported by a renewed contribution of the stimulating energy, whose reserve is soon exhausted, suffered a notable diminution. Abélard, that brilliant poet, wrote not a single strophe after he had been castrated at the age of forty by order of Héloise's cruel uncle, Fulbert. These phenomena may be even better observed in the cases of debilitated old men who, in reality, are physiological castrates, devitalized by the exhaustion of years. When their sex gland ceases to function, when they have lost the ardors of affection, a characteristic modification of their physical, moral, and intellectual condition takes place, which their families and friends are quick to note. Even

those of an affectionate disposition become egotists, make everything turn about their own precious persons, and are indifferent to occurrences which previously would not have failed to move them. Dr. Zambacco Pasha does not exaggerate greatly when, in speaking of old men deprived of the amorous function—which is only one of the numerous manifestations of the atrophy of the sex gland—he affirms that apparently altruistic acts on the part of these old men (worthy of all praise, incidentally, because of their beneficent effects) are not, as a rule, the result of a spontaneous impulse of kindness; but entirely prompted by personal interest in the hope of a reward in the hereafter, or by a feeling of worldly vanity seeking to immortalize their name in the memory of those who survive them. Such old men, with intellectual faculties on the decline, usually regard themselves as infallible, live in their recollections of the past, and allow obstinacy to take the place of intelligent decision. The great deeds of life, its noble and generous actions, occur

during the period of sexual activity, which the testicle also nourishes. How right was Metchnikoff in saying that a man of genius loses much when he loses the sexual function! If Goethe, that universal genius, produced admirable works to the very end of his days, if at the same time he evinced an astonishing degree of physical activity and energy, even during the last years of his long life, it was because he was able to fall madly in love with a young girl of nineteen, at the age of seventy-four, and, dying at eighty, bid adieu to the world with the words: "See what a charming woman's head that is, with black curls against a black background!" This great genius was a great lover, like Victor Hugo, like all other geniuses, though none but the poets among them have dared to tell the tale of their loves. The case of Goethe, the genius, at any rate, is that of all men who, reaching a very advanced age, continue to show themselves sturdily active, mentally clear, full of affectionate and generous feelings. Their sex glands still retain a suffi-

cient number of active cells, and nourish their love of life, in contrast to the old men whose glands have atrophied.

In the manifestation of his physical and intellectual qualities, varying according to the individual, man himself is worth whatever his sex glands are worth.

The case of the eunuchs proves this conclusively. All their organs are absolutely identical with our own, one only is missing. Yet the fact that they have been deprived of this one organ lowers and enfeebles the function of all the rest. Hence, while he has the same brain, the same heart, the same muscles, the eunuch is a creature fallen and decayed, since all his organs, lacking a vital stimulant, do their duty in a manner slack and remiss, and become incapable of guaranteeing the individual an average span of existence.

CHAPTER V

The experiments of Brown-Séquard—The failure of his method is due to defective means though at the service of the right idea—A legend of the Middle Ages regarding the grafting of organs—The grafting of a young sex gland, in full activity, means incorporating in the organism the very source of our vital energy—My report to the 28th French Surgical Congress on the grafting of testicles—The grafting of testicles upon normal males, upon castrated males and upon aged senile males—The grafting of these glands upon females—Disappearance of the infirmities of old age—Restoration of the powers and rejuvenation of senile animals—Prolongation of their life—Remote results of testicular grafting—The possibility of securing these glands from men killed by accident or from executed criminals—The need of making legislation conform to the actual progress of science.

THE study which we are making of the part played by the sex gland shows that, contrary to the other glands, which excite or moderate the activity of a limited number of organs, the sex gland influences the organism as a whole.

The sex gland stimulates cerebral activity as well as muscular energy and amorous passion. It pours into the stream of the blood a species of vital fluid which restores the energy of all the cells, and spreads happiness. and a feeling of well-being and the plenitude of life throughout our organism. The period of its greatest activity corresponds to the greatest expansion of all our faculties. It is the moment when our ebullient brain and our over-stimulated energy incite us to the most daring actions. The idea of capturing this marvelous force, of placing it at our service when its natural source begins to dry up as we advance in age, had haunted my mind for a number of years, ever since my studies in the case of the Egyptian eunuchs had revealed to me all the importance of the internal secretion of this gland.

Brown-Séquard had already given thought to it. In fact, this celebrated physiologist had informed the *Académie de Médicine,* in 1889, with all the weight of his authority, and an accent of profound conviction, that having

had an injection obtained from the glandular sac of the ram by means of the trituration of the sexual organs of the animal in question administered to him, he had, at the age of seventy, recovered the force and energy of youth, with manifestations unknown to him for a number of years. This declaration, as one may well suppose, made a tremendous impression on the learned body to whom it was addressed, and was soon spread abroad throughout the entire world. The newspapers got hold of it, and the reviews published at the end of the year spared the great scientist no more than they did myself, after I had made my report to the Surgical Congress.

The almost universal application of the Brown-Séquard method has not, however, realized the hopes which were entertained for it, and at present it has been almost entirely abandoned. Nevertheless Brown-Séquard's affirmation was exact, and his belief that a source of vital energy had been discovered in the sex glands was true and correct.

What warped the resulting application of

the theory and multiplied miscarriages was the therapeutic process employed in order to introduce the production of the secretion of this gland into the organism.

In the first place, it must be observed that the trituration of the organ does not allow us to extract from it its entire product, the liquid thus obtained always being deficient in its *active element*. The little thus obtained may, however, still produce good effects if it be injected as soon as the manipulation has been terminated, which Brown-Séquard did. But everyone has not a biological laboratory at his disposal. Now this liquid, like all organic liquids, changes very rapidly, loses its properties and may even become toxic. The process of leaving the laboratory to enter the shop of the pharmacist, causes the loss of what has remained of its virtue in the transit, which accounts for the failure of the method of its actual abandonment. A poor process placed at the service of a good idea has done the idea itself disservice. Yet this is no reason for adding to those eulogistic epithets which are

always showered on the illustrious scientist, that of being a man of impulse. His impulsion was generous and his idea was right. But at that date scientists did not as yet know of better methods for making this idea practical. Brown-Séquard's mishap as regards the sex gland has none the less contributed to install a new method in medicine: opotherapy. And though it has not been possible to utilize the subtle liquid of the sex gland in the manner shown, the products of the thyroid gland, the suprarenal gland, the pituitary gland, have been found to lend themselves perfectly to local ingestion or use in the form of subcutaneous injections. Since then science has advanced. Humanity, its intelligence on the alert, has made new conquests. The daring idea of compelling borrowed organs to live again in our own bodies was born, or better said, realized, for the idea itself is not new.

In fact, there is a legend of the Middle Ages which tells of the miraculous cure of a pious guardian of the church of Saint Peter in

Rome by means of a graft practiced by the venerable Saint of the said church in person. After having amputated a leg devoured by a cancer, he replaced it with that of an infidel, whose mutilation was hardly worth mention, seeing that his body, at all events, was fated to roast in hell-fire. This medieval legend in its turn, can be none other than the echo of far older legends. Hence this is an ancient, a long-cherished dream of humanity which our own age realizes at last.

Cast aside one's old organs like worn clothes in order to replace them with new organs, what a beautiful dream it is indeed! Three French scientists in particular have endeavored to put it into effect: Paul Bert, Ollier and Carrel, among a whole galaxy of investigators, have contributed so many convincing facts during the past few years that grafting has become a part of current practice.

Hence, when once I understood all the importance of the part played by the sex gland, when I had come to realize that its internal secretion stimulates the vital energy of

all our tissues, the decay of which is the primary cause of our old age, the grafting of this organ was the first thing that entered my mind.

The grafting of a young sex gland, in full activity, means incorporating in the organism the very source of our organic action. Thus the body would be supplied, not with a dead product, incomplete, often changed, introduced from time to time by means of subcutaneous injections, but a living organ, carrying out its functions itself. To graft this gland is to place it in direct communication with our blood-vessels, which will undertake to transport the precious fluid in proportion to its formation in the intimacy of our tissues. To graft this gland is to participate at first hand in the work of creation, to imitate Nature in the procedures which she has elaborated in order to insure the harmonious functioning of our body.

I was encouraged in my task by previous experiments which I had made with ovaries, and which had proved to me that it was pos-

sible to undertake the grafting of glands whose structure was at least as delicate as that of the sex gland. I had, in fact, communicated the convincing results of my ovarian grafts to the *Congrès Français de Chirurgie,* in Paris, in 1912, and to the "International Congress of Medicine" in London, in 1913, and as regards the latter, I was able to show them the lamb born of an ewe whose ovaries I had removed, replacing them with the ovaries of her sister. However, the hope of succeeding in the graft of the sex gland did not as yet justify the practice of this operation on man. The most solidly established hypotheses are only valuable in degree as their correctness has been verified by experiment. First of all, facts must be allowed to speak for themselves, and we must bow to their verdict. Hence, I undertook, in the beginning of the year 1917, a series of experiments which were to clarify my beliefs, and I did not communicate the results obtained to the *Congrès Français de Chirurgie* in Paris until October 8, 1919.

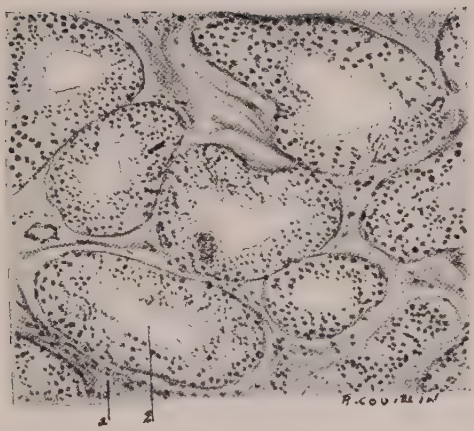

FIG. 12.—HUMAN TESTICLE (ADULT)

It shows the canaliculi surrounded by the interlobular conjunctive tissue (After *Précis d'Histologie*, by A. Branca).

I will, in the first instance, reproduce this report as it stands:

"Testicular Grafts

"*An Experimental Study Made at the Physiological Laboratory of the Collège de France.*

"For over two years, in my laboratory at the Physiological Station of the *Collège de France,* I have been conducting experiments in testicular grafting, in collaboration with my wife, Mme. Evelyn Voronoff, assistant at this laboratory.

"We have in this graft in no wise endeavored to preserve the spermatozoic functioning of the testicle necessary for the species, but solely the stimulant effect of the internal secretion necessary for the individual himself, in the same way as the internal secretion of the other endocrane glands.

"Our experiments have been carried out on a whole herd of sheep and goats of which I

am still keeping some fifty or more at the Physiological Station of the *Collège de France,* at the *Parc des Princes.* I chose these animals because, in their case, sex is at once recognizable owing to the development of secondary characteristics, contrary to what may be observed in the case of dogs, rats, guinea-pigs, etc. Besides, as you know, Marshall, and Cornevin as well, experimenting on rams and he-goats, have shown that castration when practiced at an early age prevents the appearance of horns, and, when the operation has been practiced after puberty, the existent horns cease to develop and take on the appearance of slight, female horns. A change also takes place in the conformation of the head, which grows smaller, in the legs, which become longer, and in the general appearance of the male.

"In the same manner the old ram, castrated, so to speak, by the advance of age, in losing his sexual ardor loses at the same time his vivacity and his combative instincts.

"All these considerations have induced us to

make a preferential choice of the ovine race for our experiments.

"Testicular grafting has been practiced in a number of cases practically equal upon normal males, upon castrated males, upon normal females, upon castrated females, and upon very old, exhausted and enfeebled males, incapable of reproduction.

"It is impossible, in the course of the few moments allowed by rule for each report, for me to present in detail the 120 experiments which I have carried out, as well as the numerous histological examinations of grafted testicles made at the *École de Médicine,* by the eminent histologist M. Retterer. These last will furnish the subject of a report by M. Retterer himself to the *Société de Biologie.* I will confine myself, for the moment, to outlining as succinctly as possible the experiments themselves.

"I have grafted complete testicles twenty-five times; large fragments, fifty-eight times; very small fragments, thirty-seven times. Transplantation was effected subcutaneously

sixty-five times; in the sacs, thirty-two times; and twenty-three times in the peritoneum.

"In no case has direct vascular anastomosis been practiced, something, incidentally, incapable of realization in view of the slenderness of the artery and of the spermatoid veins. Happily, anastomosis was not necessary. The testicular tissue possesses a remarkable aptitude for transplantation. The examinations made by M. Retterer of graftings removed at the end of one, two and three months, a year, and fourteen months, place this beyond all doubt. It is the peripheral portion of the glandular substance which survives, the central portion which usually loses its vitality.

"Grafts in the bag, in the vaginal tunics, furnish results far superior to those offered by grafting under the skin or even under the peritoneum.

"The histological examinations of entire testicles and testicular fragments by M. Retterer, show at the same time that the vitality of the graft under favorable conditions may be just as well insured by the one as by the

other method of grafting, especially if the albugineous tunic is very slender. The percentage of successes is, however, very much higher when fragmentary transplantation is practiced, which is readily explained by the fact that the nutrition of the small fragments may be assured more easily than that of an entire testicle.

"Besides, our aim being to implant in the tissues glandular cells elaborating internal secretions, whether they be transplanted wholesale or divided into small groups is not material. In fact, the testicles, either transplanted entire, or divided into small fragments, have just as comprehensive an influence on the organism as the normal testicle, and, as we shall learn, call forth again the physical and psychic characteristics annihilated by castration or old age.

"In the case of females I have, on the contrary, not observed any marked influence resulting from grafting, unless it be a certain arrested growth of the long bones. The she-goats and ewes, normal as well as castrated,

remained very vigorous after the graft, but did not attain the size of the comparative subjects (Fig. 13). I have not been able to observe the appearance of the secondary characteristics of the male, such as the thick horns, and the male sexual instinct. On the contrary, the presence of the testicular fragments seemed to disturb their instincts. When they give birth to young, in most cases they refuse to suckle them, and regard them with a kind of surprise and indifference which speaks for the abolition of the maternal instinct.

"In the photographs which I offer for your inspection, of the he-goats, Nos. 69, 17 and 15; the first, six months of age, the second, fifteen months of age, and the third a little over two years old, you will remark that all three have magnificent horns, such as are never seen on castrated animals. (Figs. 14, 15, 16, 17 and 18.) Well, the first was castrated four months ago, the second has been castrated for more than a year, and the third for sixteen months. They have developed like normal males, thanks to the testicular tissue which I have

FIG. 13

She-goat, two and a half years old, on which the testicles of a young he-goat have been grafted. She has remained small in size.

Fig. 14
Small he-goat, No. 69.

FIG. 15
Small he-goat, No. 69, four months after the graft.

Fig. 16
Young he-goat, No. 17.

FIG. 17
Young he-goat, No. 17, one year after graft.

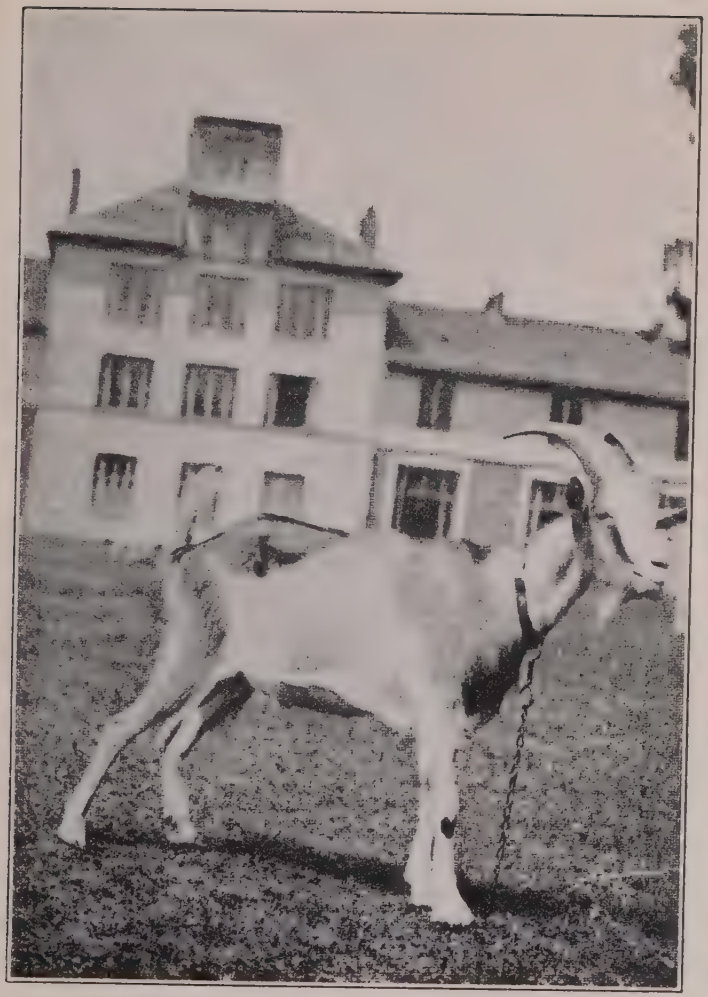

FIG. 18

He-goat No. 15, sixteen months after grafting. He had previously been castrated at the age of six months.

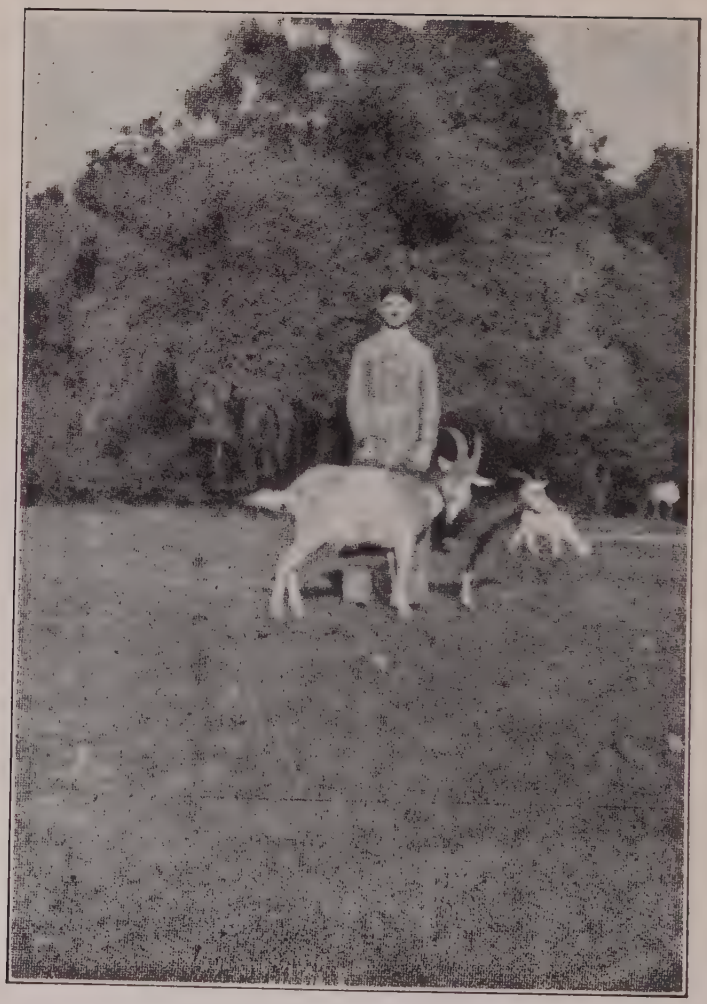

FIG. 19

He-goat No. 15, completely castrated at the age of six months, testicles taken from another young buck having been grafted on him.

FIG. 20
Castrated he-goat No. 15.

FIG. 21
Castrated he-goat No. 15.

FIG. 22
Castrated he-goat No. 15.

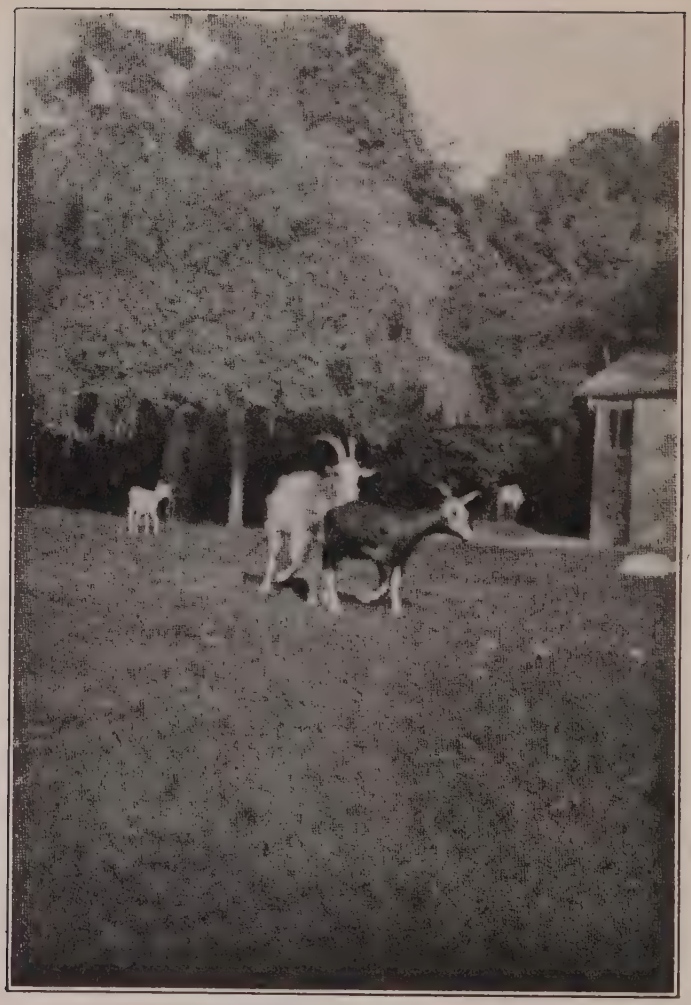

FIG. 23
Castrated he-goat No. 15.

grafted on them, immediately after their castration.

"The effect of the graft is shown not alone in the growth of the horns, but by the appearance and behavior of these animals as well, for they are lively, vigorous and belligerent, and do not grow fat. No. 15, actually two years old, shows sexual ardor besides, running after the females quite as though he had suffered no removal of his genital organs. Various attitudes, as caught by the camera, offer the most convincing proof of this. (Figs. 19, 20, 21, 22 and 23.) Still more remarkable is the effect of grafting on the old rams, photographs of which I can also offer you.

"One, No. 12, was brought to me in a deplorable condition, as you may verify by the photograph taken on the day before the operation (Fig. 24). At twelve or fourteen years of age, which corresponds to the age of eighty or ninety in man, the goat tottered on his legs, suffered from inability to retain his urine, due to senile decline of the vesicular sphincter, and gave the impression of an animal exhausted

by age and very near the term of his existence. On May 7, 1918, I grafted in the right vaginal tunic, above his own testicle, four large fragments, representing an entire testicle removed from a young ram. Two months after the graft had been effected, the animal was completely transformed. His urinal incontinence had disappeared, so had the trembling of the legs, and he no longer looked afraid. His bodily carriage had become magnificent, he behaved in a lively, aggressive manner. The old ram had taken on the appearance of remarkable youth and vigor (Fig. 25). He was isolated in a small stable, together with a young ewe-lamb, which afforded an opportunity for observing not only the awakening of his sexual instinct, which he had lost years ago, but also the following more tangible result: the ewe-lamb covered by him in September, 1918, dropped a vigorous lamb in February, 1919. There is nothing in the fact to cause surprise. Old animals, like very aged men, occasionally still possess spermatozoids which are altogether alive, but it is the atrophy

FIG. 24
Old ram, No. 12, before grafting.

FIG. 25
Old ram, No. 12, a year after grafting.

of the internal secretive cells which prevents their experiencing the sexual appetite and manifesting their virility. This old ram, No. 12, not alone made it possible for me to verify the prodigious effect of the graft, but the disastrous effect of its disappearance as well.

"Wishing, as a matter of fact, to acquaint myself with the structure of the grafted gland at the end of a year's time, I removed it and confided it to M. Retterer for histological examination.

"Three months after the removal of the graft, I was informed that the ram which had been so savage, was aging with disconcerting rapidity, that he had once more grown gentle, indifferent and timid. In fact, I was obliged to admit that there was hardly a trace left of the youth he had regained. I then essayed another graft upon him, on June 7, 1919, and its effect did not delay in manifesting itself. Once more I had before me a superb animal, carrying his head high, and again full of affection for his companion.

"Thus I have been able to verify what a

potent effect the internal secretion of the testicle exercises on the organism, and what advantage may be taken of it.

"Would it not be possible, when that evil, old age, the state of senility, is due to an insufficiency of the internal secretion of the testicle, to combat it as one fights a malady, by restoring the source of its vigor and energy, which age has dried up, to the body?

"Would it not be permissible to suppose as well that it might be possible, in the same cases, to prolong life itself, which would be in no way surprising, since the surgical castration, or physiological castration due to increase in age for the most part abridge the term of our existence. Eunuchs rarely reach an advanced age, and as for my old ram, No. 12, two years ago he had no more than a few weeks or months of life left, a life of wretchedness. At present he would surprise you by the vital energy and youthfulness which all his movements betray. One is given the impression that with each new graft he receives a

FIG. 26
Old ram, No. 14, before grafting.

FIG. 27
Old ram, No. 14, a year after grafting.

new fountain of vitality, and that his strength renews itself.

"I have repeated this experiment on several other animals—castrated as well as afflicted by age, and the result has always been the same. Subject No. 15, already mentioned, also fell into a decline at the end of fourteen months, when I had also removed the graft in order to confide it to M. Retterer. A new graft practiced upon him on April 22, 1919, restored his virility and his vital energy. No. 14, a ram quite as old and wretched in 1918 as No. 12 was at first, once more, in 1919, became superb, with all the spirited impetuosity of an animal running over with strength. Compare the photographs taken just before the operation and those taken a year later. They constitute the finest possible demonstration of the effect of the testicular graft (Figs. 26, 27).

"I might multiply these examples, but a visit to my laboratory would be far more satisfactory and would allow you to seize at a glance the tangible results which I have obtained.

"The injections of testicular juice have not had the result which Brown-Séquard expected from them, because the glandular extracts undergo rapid changes, do not contain the whole of the product of the internal secretion, and are even, at times, toxic, as M. Gley, the eminent professor of the *Collège de France* has proved.

"Grafting, on the contrary, in incorporating the gland itself in our organism, allows it, as long as its vitality lasts, to continue to pour its active products into the blood.

"The endocrinal glands are powerful workshops wherein are elaborated the substances which ensure the proper balance of our functions.

"The deprivation of the minute parathyroid glands, or of the suprarenal glands, never fails to cause death; the absence of the thyroid gland produces cretinism; the lack of the internal secretion of the testicle determines impotence, and physical and moral decline.

"To make up for their lack or for the insufficiency of their functioning by the grafting

of a new gland would be a noble ideal of attainment in human therapeutics."

More than a year has elapsed since this report was made, and the results which I made known to the Congress have not only been sustained, but new facts have been added to them. The ram No. 12, already a father after grafting, is now the parent of a second lamb, dropped February 22, 1920. The ram No. 14, isolated in the same manner with an ewe-lamb for eighteen months, is the father of a lamb in turn. All the animals are enjoying the best of health, and up to the present there is nothing to indicate a return on their part to the wretched condition in which they were before grafting. Whether or no my opinion as regards the rôle of the sex gland be accepted, the fact remains, one easy of verification, since the grafted animals are always kept at the Physiological Station of the *Collège de France.* It is easy to establish their ages, the veterinaries have the precise record. Several among them have exceeded the age-limit which

animals of their species attain, and instead of showing signs of decrepitude, of old age, of senility, which no animal arrived at the term of its existence escapes, they give proof of an absolutely astonishing vigor and fervor of life.

How long will this last? When will the moment arrive for this new gland to be in turn attacked by atrophy and cease to exercise its stimulating effect upon the organism? I do not know. The future will tell. But what I can affirm is that some for two years and others for three have enjoyed good health which they did not possess during the years immediately preceding the graft, that some among them have procreated young, something they had been altogether incapable of doing for a long space of time, and that instead of pitiful beasts, timid and dejected, showing the marks of senile decrepitude, they have once more become superb animals, full of spirit, aggressive and belligerent. And since I have seen them in their wretchedness, and the only treatment given them has been

the grafting on them of sex glands taken from young animals, I am convinced. I know that inventors readily confuse their desire with realization, and that in all sincerity, by a sort of auto-suggestion, they behold as fact what, actually, has only transpired in their imagination. This, however, cannot be the case here. The dropping of a lamb in a stable where for a year and a half an impotent old ram, tottering on its legs, suffering from urinary incontinence as a result of extreme old age, has been shut up with a young ewe cannot be regarded as auto-suggestion, any more than the disappearance of the ram's urinary incontinence and the trembling of his legs. It is equally impossible for me to admit any error of interpretation when I see the picture—fixed by my camera—of an animal castrated at the age of six months, and grafted a year later, showing an amorous ardor to which the female is complaisantly lending herself. I am similarly obliged to realize that I actually have in my possession animals which have passed beyond the extreme limit of their lives. There

was nothing in their lamentable condition before grafting which might lead me to anticipate this exceptional longevity. I do not know whether all these facts will convince the incredulous. I have been told that the members of a learned society declared the inventor who brought the first phonograph to their attention to be a ventriloquist. In addition to those who are malevolent, jealous and envious, one must always allow for those who are repelled by anything that is new. They will not accept it save in order of seniority and when it returns to them, like a veteran, with well-merited service-stripes. In any case, my conviction is assured, and that is enough to induce me to think of applying to man a method by which hitherto animals only have profited. Yet here a great difficulty arises. In order to restore force and energy to debilitated animals, I have removed from young ones what was lacking in the old, and allowed the latter to benefit at the expense of the former. Such a procedure is impossible of application in the case of man. It would in fact, seem little charitable to de-

prive some young creature of a source of energy that an aged man might profit thereby, though, in certain exceptional cases, it might be desirable. The restoration of the vital energy, the productive power of a Pasteur, may well be worth the slight mutilation inflicted on a robust porter. I say slight, because, in reality, only a single gland is grafted, which is amply sufficient for him who receives and does not impair him who gives it. But men would rather have one of their eyes removed than to yield up one of their glands; and the two offers of the sort which I have thus far received were by no means dictated by a feeling of altruism. At the figures at which these persons have estimated their precious glands, grafting would be accessible only to millionaires, and it is not always among these that we find the existences that it is most desirable to prolong and intensify. Hence the future of my method would be seriously compromised if this were the only resource existing to obtain young glands for purposes of grafting. Fortunately, it will be possible to obtain them

more cheaply, when the day dawns in which physicians will be authorized to remove these organs from healthy men, killed by accident.

Death, in fact, the stoppage of the heart, does no more than break the functional harmony of the organs. The individual himself, as an acting, conscient being, able to express life in his collective entirety, is dead; but the various tissues which compose his body do not die at the same time, and several among them survive for hours. The epidermis retains its vitality long after death, and one may see the hairs of the beard growing on a corpse. The bones survive for eighteen hours, and if removed before, retain all their vitality. The other organs, according to their structural delicacy, give evidence of life for a longer or shorter period, but invariably for a period shorter than in the case of the epidermis and the bones. The brain is the first to succumb; yet not swiftly enough to prevent the head detached from the body of an executed man from finding time to realize its horrible situation,

agreeable to the laws of man, but contrary to those of nature.

Removed before their own individual death, these organs retain all their energy, all their vital properties, and, transplanted into another body, are able once more to carry out their original functions. And even more, when these organs are removed in time, they may be kept alive for weeks if preserved in refrigerators where the temperature is maintained at zero. In all great cities the accidental death of young and robust individuals is recorded day by day. Nothing could be fairer than to remove their organs, if it is certain that the organism is a healthy one, and place them in refrigerators in order to be used as the need arose. In every large city a special hospital should be instituted, where those might be brought together in whose case the grafting of an organ might ensure continuity of life, restoration of vigor, or the conservation of some important function or faculty. Every young person who has died by accident, should at once be transported to the hospital

in question, and his organs, after an attentive examination, should be removed, properly preserved and utilized.

Unfortunately, prejudice and legislation are still opposed to this. The custom of centuries insists that we return the mortal remains to earth, where they are slowly and uselessly consumed. But time will accomplish its work, the evolution of feeling and law will follow the evolution of science, and sentimentality will be replaced by the lofty consciousness of a superior duty: the service of humanity even after death. For the rest, even to be reborn in part only, to become a new integral portion of some living being, would it not be a fate more enviable than cold dissolution at the bottom of a tomb?

While waiting for that time, which I do not despair of seeing arrive, we cannot count upon those treasures of life which are the legacy of the dead. It would, perhaps, be easier to obtain an authorization to remove the sex gland from men condemned to death, after their execution.

We cannot, however, at least for the time being, rely on the human gland for grafting purposes, save in very exceptional cases. Is the method, therefore, fated to remain unborn because of a lack of material to supply it? Will humanity be deprived of one of the most powerful means of infusing it with renewed energy when that with which nature has dowered it begins to fail? I trust not. Fortunately we have a near relation in the animal world from whom we may borrow what we need with less scruple.

CHAPTER VI

The possibility of borrowing the sex gland of the higher simians in order to graft it on man—Man's relationship with the higher anthropomorphous simians—Resemblance between the simian and the human fœtus—Identity of dentition between ape and man—Analogies between skeletons, skulls and internal organs—Blood-relationship—The relationship established by the fact that the apes enjoy the regrettable privilege of being the only animals who contract our diseases: typhoid fever, syphilis, etc.—Success attending the grafting of the thyroid gland of the ape on man—The very favorable secondary results of similar graftings—The far more pronounced success attending the grafting of the thyroid gland of an ape on a man, than produced by man to man graft of this gland—The future of grafting simian glands on man—Application of the same method to intensify female life—Methods for securing their esthetic rejuvenation—The drawbacks of some of these graftings so far as women are concerned—Effect upon the organism of the deprivation of the internal secretion of the ovaries—The grafting of youthful ovaries, in full activity, on aged women.

These relatives of ours are the higher simians, the anthropomorphous apes — the orang-outang, the chimpanzee and the gibbon.

Everything brings us nearer these younger brothers of ours, and our close relationship to them is shown from the very first days of the development of the embryo. Selenka, who is best versed in the embryology of the apes, observes that at first it is almost impossible to distinguish the human embryo from that of any ape. Later, the fœtus of the higher simians comes to resemble that of man far more than it does the fœtus of the inferior simians. The three-months' fœtus of a gibbon, of which Selenka has supplied the picture might just as easily pass for that of a woman. The differentiation is not stressed until later; yet even at five months the resemblance is still notable, as may be verified by the figures given by Denniker and Buffon regarding five-month fœtuses of the gorilla and the ape. Denniker has been able to verify that the gorilla fœtus has actual hair only on its head, forehead, and about the lips and genital organs, without

counting eyebrows and lashes. The remainder of the body was smooth or covered with a hairy down no more than a thirty-ninth thousandth of an inch long. According to Selenka, who regards the gorilla as our nearest relative among the simians, "the great resemblance of the premolars and molars in the chimpanzee's final dentition to the human teeth, seems to indicate that the chimpanzee and man have a common origin, and descend from extinct forms."

In fact, we know that in the comparative study of mammifers, the dentition supplies one of the most decisive characteristics for the determining of the analogies or differences among the various species, and Selenka's observation is a very significant one. Incidentally, Huxley, in his masterly work, "Man's Place in Nature" confirms that "whatever difference as regards dentition the highest type of ape may offer as compared with man, these differences are far less considerable than those which may be verified between the dentition of the superior apes and the inferior apes."

However, these differences apply only to the strongest dental development among the apes, though they have the same number of teeth (32 in adults) and their milk-teeth are identical with our own. The analogy between the skeleton and the skull is very marked, as also between the muscles and the internal organs. They are afflicted with the same inconvenience as ourselves in the possession of an appendix similar to our own. Even with regard to his brain the chimpanzee is much nearer to us than to any one of the inferior apes. And if he does not possess an articulate language, it is because of the lack of development of his laryngeal muscles. Yet what should carry conviction of the fact that man is united to the superior apes by the bonds of a close relationship to the most incredulous, is the verification made by Gruenbaun, of Liverpool, and since confirmed by other scientists, that the blood of man is absolutely similar to that of these apes and differs completely from that of any other animal.[1]

[1] Gruenbaun and Bruch discovered this actual blood-rela-

This physiological relationship is still further confirmed by the pathological one, and it is only the apes who enjoy the sorry privilege of contracting our maladies, such as typhoid fever and syphilis.

The miracle by means of which a common ancestor gave birth to two children who have followed such divergent paths in their ulterior evolution, does not come within the scope of our considerations, any more than does the elucidation of the mystery owing to which common-place children and such geniuses as Newton, Pasteur and Michelangelo come to be born in the same family. What is important to remember is that it is logical to admit in advance that the organ of an ape transplanted into the body of a man will find there the same conditions of life, the same nutrition available in the case of its first host, and that it will be

tionship by treating the serum of man and of the ape in different ways, inspired by recent bacteriological research as regards the properties of serums. Thus the serum of the rabbit prepared with the human blood does not precipitate any animal serum whatever, except that of the inferior apes (a light precipitation), while with that of the anthropoids it precipitates almost as abundantly as with the human serum. For his part, Bruch of Batavia, using the method of deviation of the complement, has secured the same results.

able to adapt itself to its new existence amid these surroundings with which it is familiar.

I myself know, better, perhaps, than anyone else, by reason of my long practice in grafting and the experience acquired during the war, at the "Hospital of Bone Grafting," that a graft taken from a man himself, or from another man furnishes the best and most certain results. I am the first to condemn vain attempts to graft the organs of calves, sheep, etc. It has already been proved, and I have shown at length in my *Traité des Greffes Humaines* (Treatise on Human Grafts) that the thing is absolutely impossible. Between the animals and ourselves yawns a biological abyss, and none of their organs is able to survive in our body. Yet if man may be qualified by Huxley as a talented ape, might not the ape deserve the appellation of a primal man? In any case the similarity of our tissues and our blood to that of the superior apes is such that the grafting of a simian organ on a man may be compared to that of a graft from man to man. Besides, some observations have already been made

which confirm the actuality of the fact. The report made by Professor Kuttener to the Surgical Congress of Berlin, in April, 1913, is very characteristic. It concerned a child in whom the fibula was congenitally missing, and on which Kuttener had grafted the fibula of an ape. The operation had been made eighteen months before. Radiography has proved that the bone had stayed in place without the least trace of resorption. One might, notwithstanding, object that in this case it was merely a question of a simple, resisting organ, of a bone, offering only a slightly marked differentiation and occupying an inferior place in the organic scale. But I was glad to be able to offer on June 30, 1914, the *Académie de Médicine* a new statement of fact, this time bearing on the graft of one of the most delicate and perfected organs we have, and which is in every way comparable to the sex gland with which we are dealing. I transplanted the thyroid gland of an ape into the neck of a child with a degree of success which exceeded my best hopes. The importance of the fact is so

great, the road it opens up for the future of grafting is so broad, that it seems worth while to reproduce at least the essential part of the report in question:

"The case in question was a boy of fourteen, Jean G——, born of Corsican parents whose thyroid mechanism was devoid of any blemish; nor did their ascendants present any indications worthy of remark under this head. Two other younger children are entirely normal. However, the little sufferer at first seems to have been a well-made child. He was born at the appointed time, began to walk at nine months and speak at twelve. Nevertheless, despite his precocity, the child was somewhat calm and apathetic. Nothing especially worth recording occurred until he was eight years old, unless it were the persistence of his apathy, the slowness of his movements and his want of interest in play. At this period the child had the measles, and immediately following this disease the symptoms which attracted the attention of his parents were observable. The child's face, belly and legs began to swell;

at the same time his growth, which up to that time had been practically normal, stopped and remained absolutely stationary for the space of a year. His intelligence, which hitherto had differed little from that of other children of his age (he had begun to learn to read and write) also ceased to develop for a time. His teacher and his parents noticed that the boy made no further progress, that he was becoming increasingly dull, deaf, and articulated his words with difficulty. Dr. Georgi, of Bastia, consulted at this time, treated the child for albuminuria. The child possessed a quantity of albumen which varied considerably from one month to another. After two years of a lacteal diet the albumen disappeared, but the œdema continued to persist, and the child's intelligence as well as his growth remained stationary. At this time the family being in Pisa, consulted Dr. Carazani, professor of internal pathology at the *Facultà* of Pisa, who soon diagnosed a case of myxœdema in the child, whose thyroid apparatus, probably congenitally ill-developed, had suffered an infec-

tious alteration connected with the measles, incidentally quite a frequent cause of myxœdema in early infancy. Dr. Carazani's diagnosis was soon confirmed by the results of the thyroid medication, in the form of thyroid tablets, administered in doses of two per day, for a period of three months, in the Pisa hospital. The œdema of the face, belly and members suffered a notable decline. The boy's growth once more in a measure began; his hair, which was scanty, brittle and lusterless, grew more abundant and more supple; his skin, which had been scaly and dry, became smoother and softer; and his intelligence also awoke. Unfortunately, as soon as the treatment was interrupted for a couple of weeks, the boy's complexion once more turned yellow, the inflation reappeared, and he again became apathetic and drowsy. The thyroid treatment was resumed, but each time it was suspended, the same phenomena were displayed, greatly to his parents' despair. Besides, the thyroid medication, while largely ameliorating the child's condition, did not succeed in effacing the troubles

due to an insufficient thyroid secretion. His complexion remained yellowish, his lids swollen, his nose thick, his face inert and drowsy, his cheeks flabby, his eyes dull, his speech dragging and hesitant. At school, where he had been able to return, thanks to the thyroid treatment, he did not share in the sports of the other children, made little progress, and displayed a degree of intelligence far below that of children of his own age, complaining of a sort of heaviness—a weight on his head. It was at this time that I saw the child with Dr. Hobbs, a professor accredited to Bordeaux, to whose courtesy I owe the observation which I am about to relate. The child, who had stayed for some time in the country, once more interrupted his treatment, and appeared before me with the imbecile myxœdematic facies which is so very characteristic (Fig. 28). I then suggested grafting a portion removed from the gland of the father or the mother of the child itself; yet despite the affirmation of the parents that they would rather see their child die than to keep him in

FIG. 28

Jean G., aged 14 years. Photograph taken the day before the operation.

Fig. 29
Jean G., a year after the operation.

such a condition, my proposal was received without enthusiasm. I then decided to graft on this child the thyroid gland of a great Papion ape which I had in my laboratory. The operation took place in Nice, at the Sainte-Marguerite clinic, on December 5, 1913, in the presence of nineteen physicians, among them Drs. Grinda and Schmidt, the surgeons of the Saint-Roc hospital, and Dr. Roux, surgeon of the Lanval hospital. The veterinaries Duguet and Grognart were also present. In operating on the child I was assisted by Dr. Hobbs. Drs. Giovani and Fosse administered the chloroform to the ape and the child respectively.

"The operation was first undertaken on the ape, a single lobe of whose thyroid, together with its corresponding parathyroid it had been my original intention to remove. Unfortunately, the left lobe when removed, was placed by mistake in Ringer's liquid which was too hot, and I was obliged to remove the right lobe, which finally served me as a graft. This circumstance, that I had to remove the ape's

whole thyroid apparatus, together with its parathyroids, caused the animal's death from tetanus in four days. The right lobe and its parathyroids, removed with all the precautions dictated by the most rigorous asepticism, was placed in warm Ringer's liquid, to wait until it should be carried to the child. The interval was not long, for the child had already fallen asleep in the course of the operation on the ape. During this interval we had ascertained that the child's medial lobe and left lobe were entirely missing, and that his right lobe appeared as a slender lamella, a somewhat dark reddish-brown in color. This most satisfactory verification supplied the key to the phenomena observed in the child's case. The ape's right lobe with its parathyroids was then withdrawn from the Ringer's liquid, which had been maintained at a temperature of about 38 degrees by Dr. Pasquetta, and was placed in the little cell which should have been occupied by the missing left lobe of the child.

"The after-effects of the operation which has been so disastrous for the ape, were, on the

contrary, most simple so far as the child was concerned. The simian gland was perfectly tolerated by the child's organism, and no elimination resulted. The success of the operation was thus at once established. It remained to discover whether this gland would merely be tolerated for a certain length of time, while continuing to be a foreign body, condemned to undergo a slow and definitive resorption, or whether the graft would really take, and form an integral part of the organism in recovering its proper functions. Time only could supply a definite answer to this question. In fact, the influence of the secretion of the thyroid gland is so powerful, and the absence of this secretion, on the contrary, produces such serious troubles, that it was only necessary to deprive the child completely of all thyroid treatment and observe him. This has been done for practically the last fourteen months. Now, so long a privation of thyroid medication has not only failed to produce any injurious result, or any aggravation of the child's condition, which, formerly, took place whenever the

treatment was suspended for no more than a fortnight, but this condition, on the contrary, has been ameliorated in a clearly apparent manner. Already, at the end of one month, a diminution of the puffiness of the face, and, above all, of the palpebral œdema occurred. The eye grew more expressive, the child appeared to be less apathetic. Yet there was no reason, at this moment, to deduce from this that the graft had been a success. In fact, the restoration of the gland, if it were taking place, would act like the ingestion of the thyroid tablets, and might produce a temporary alleviation; yet in that case, it would not have lasted long, and we would have witnessed a new decline. Nothing of the sort occurred. As the months went by, the amelioration in the child's condition was emphasized in a clear and regular manner. Little by little his face lost its yellowish color, his nose and lips their inflation, the oval of his face became visibly longer. The child's movements, so apathetic and drowsy, grew more and more lively, but it was above all intellectually that he made rapid

progress. His teachers at school were unanimous in testifying to this rapid awakening of intelligence and aptitude for study, a notable contrast to the child's previous condition, when he was numbered among the most backward in his class. The same verification was made by his parents, and by Dr. Montalti and Prof. Hobbs, to whom the boy was taken every fifteen days, and who made a note on each occasion, of the increasing mental and physical progress of his mental and physical condition. Here we have a positive fact which permits of no doubt with regard to the success of grafting the thyroid gland of an ape on a human being (Fig. 29).

"Professor Bernard, who has made a masterly study of the question in Le Dentu and Delbet's *Traité de Chirurgie,* was therefore, correct in writing some six years ago: 'that it is possible and even probable that within a few years' time, fragmentary grafting, and partial and total transplantation of the thyroid and its parathyroids will be commonly effected, with a considerable proportion of successful

operations. This would be the radical treatment, since it would once and for all provide all myxœdematics and tetanic parathyroidians with the organ they lacked.'

"Thanks to the technical process I have described, the grafting of the thyroid of the ape on man is possible, and a large number of myxœdematic adults, and, above all, children, actually lost to society, who are the despair of their parents and condemned to a vegetative life, may thus be saved."

This report, as I had presented it to the *Académie de Médicine* in 1914, and the photographs of the child before the operation, and a year later, might suffice to carry conviction with regard to the efficacy of the graft of a simian gland on a man. Yet what I am able to add at present, six years after the communication was made, far exceeds the value which I myself attributed to the fact called to the attention of the *Académie*. The boy's father, employed at the *Casino de la Jetée* at Nice, was of Corsican descent, and returned toward the end of 1914, to Bastia, in his own country. I

had lost sight of my young patient, and hearing nothing of him, in spite of his parents' promise, will admit that I considered this silence an evil augury. I thought that his parents did not send me any news because the amelioration obtained during the first year following the graft had not been able to maintain itself, that the child must have relapsed into the state of imbecility whence I had hoped definitely to have drawn him.

I experienced some scruples for having, perhaps, led the *Académie de Médicine* into error by submitting too early a report of the success of this graft. But what was my joy when toward the end of the year 1917, I received a registered letter from Bastia, which I keep carefully, as though it were a relic, in which the father of Jean G—— begged me to use my Paris connections in order to secure for his son a station less hazardous than the post of danger in the front-line trenches to which he had been assigned. Thus this little Jean, whom I had known in 1913 as a poor little imbecile, with a rudimentary brain, and the body of an

eight-year-old child, had been declared, four years later, fit for military service, and had marched off to defend his country like any other man. The ape's gland, therefore, had done its part marvelously well, and the internal secretion supplied by it not only had stimulated the growth of the bones and the development of the body in the human being, but his cerebral activity as well. It had neither atrophied nor resorbed and, actually, at the end of six years, it continued to manifest its presence and perform its functions as perfectly as the normal human gland. The proof of this fact has been adduced. This experiment demonstrates that the gland of an ape may replace that of a man and take the place of his own human gland which is wanting.

Another observation, an unpublished one, regarding a child on which I had grafted, in Paris, in 1916, the thyroid gland of a chimpanzee adds further confirmation to the fact adduced. Since then I have had a number of opportunities to practice the grafting of the thyroid gland as a remedy for cretinism and

the arrested development of myxœdematic children. But I did not have the apes, just as at the present moment I have none in order to make graftings of the sex gland of the ape on man, and I had recourse to the child's mother, removing one of her three thyroid lobes which, incidentally, did not in any way disturb her later. I made use of the mother's gland in preference to any other, by no means because it possessed greater virtues than those of other members of the family, but because it is invariably the mother who offers her own in her sublime devotion to the child whom nature has disinherited.

It is true that I obtained good results; yet they have never equaled those furnished by the ape's gland. The best I had were obtained in the case of a young man of twenty, Georges P— —, of Montereau. M. Gley, the eminent professor of biology at the *Collège de France,* mentioned this case in his address at the inauguration of the Institute of Biology of Barcelona, in 1919, after having had an opportunity to verify the progress made by the

patient three years after the graft. The photographs will demonstrate more clearly than all descriptions what a transformation the child has undergone since the grafting (Figs. 30, 31). As to progress in his mental functions, I will content myself with signalizing in this work, wherein I have no occasion to deal with this question, that before his graft, his intelligence might, at the most, be said to equal that of our domestic animals. At the age of twenty he did not know how many fingers he had on a hand, and articulated a few words with difficulty. He was operated upon September 21, 1915. At the present moment he reads well, writes passably, plays the piano and conscientiously helps his parents in their work as pastry-cooks. He is no longer a degraded creature with an idiot cast of features —he makes the impression of being a young man with an intelligent eye, who follows your conversation and answers you to the point, but —with all that he is no fighter like Jean G. . . .

His mother's gland has caused him to make considerable progress, but it has not as yet

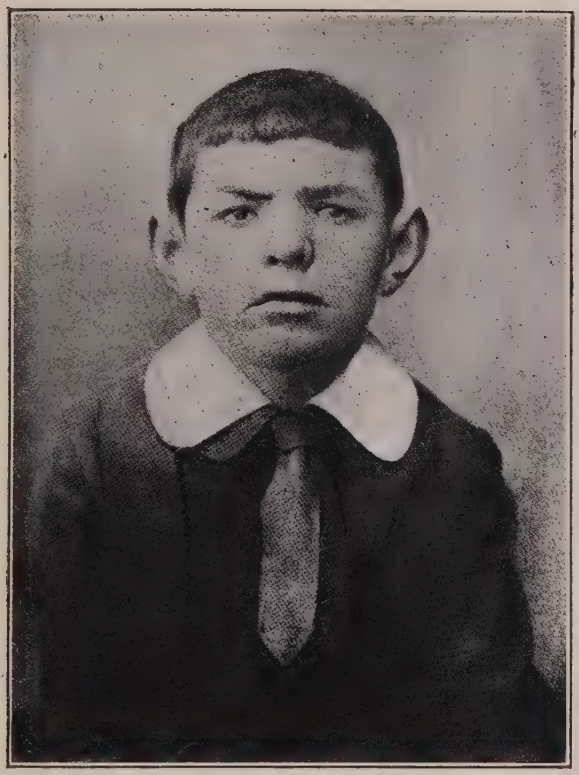

FIG. 30

Georges P., at the age of twenty. Photograph taken on the day before the operation.

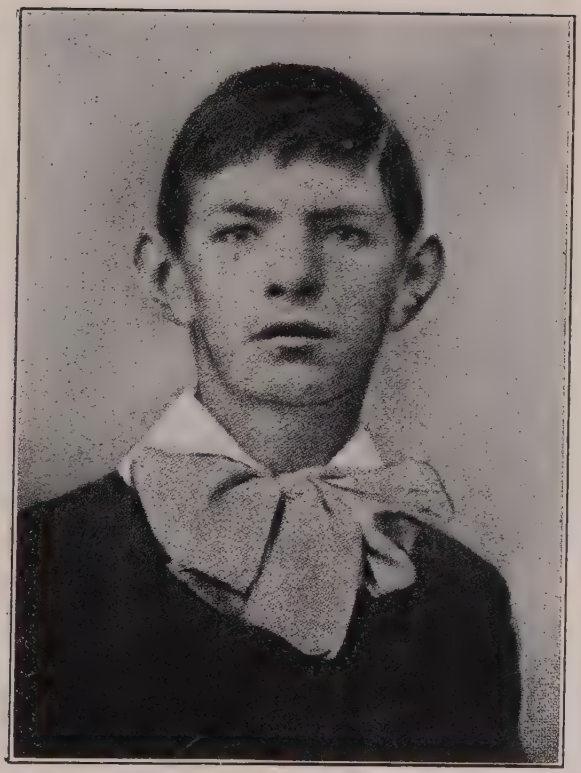

Fig. 31
Georges P., a year and a half after the operation.

allowed him to acquire mental qualities indispensable for a conscious and independent life. He still has need of the protection afforded him by his environment. The ape's gland served my first two subjects better.

The same observation applies to my last case a myxœdematous child sent to me by Dr. Lesné, physician at the Tenon hospital. The operation, performed a year ago, with the aid of a thyroid lobe removed from the mother, has resulted in the resumption of growth, the disappearance of the œdema, and the awakening of the intelligence; yet, the physical and intellectual progress made is far more gradual than that which I have observed in the case of the graft of the simian gland.

Is it because the ape is superior to man in respect to the quality of his organs, owing to a more robust physical constitution, one less attainted by hereditary alcoholism, arthritis, etc., or is the difference due to the fact that in the former cases the gland was furnished by young apes, and in the others was supplied by women approaching or having passed their

fortieth year? I cannot tell. But what is certain is that the gland of the ape when grafted on man has afforded me better results than those obtained by a human gland.

I can reply to the objection that one might be tempted to make, that I cite these two cases only, by saying that the facts would be numerous if the apes were not lacking. I even believe that if we have remained for so long a time in ignorance of the resources which the ape offers us for grafting, it is actually because these animals themselves have not been available. Scientists have frogs, guinea-pigs, dogs, and, at the most, goats and sheep at their disposal; but apes and, above all, chimpanzees, are only found as an ornament of zoological gardens, and even that is not always the case. The only chimpanzee to be discovered at the *Jardin des Plantes* in Paris, for the last six years, was the one I had installed there myself, after having removed his thyroid gland for a backward child and his humerus for a wounded man in my hospital.

Yet an even more decisive reply may be

made to such an objection. A negative result may be open to doubt, a positive, never. When in the expectorations of a patient suspected of tuberculosis, the Kochian bacilla is not found, one is not authorized to conclude that he is not tubercular, since for one or another reason this microbe might not happen to be present in the particle submitted to examination. Yet when, on the contrary, the microscope shows these bacillæ, then there is no further possibility of doubt—tuberculosis is patently demonstrated.

If the grafting of the simian gland had resulted in two failures, I would not have been justified in concluding that it was impossible to succeed in other cases, since several accidental reasons—faulty technic, lack of aseptics, etc., might have spoiled the result. It would have been necessary for these failures to have been constantly repeated in order to admit their validity. But when you establish that the graft of an ape's gland has been crowned with success, that for years it has satisfactorily accomplished its functions, nothing justifies our thinking that this graft,

like similar ones made under favorable conditions, will not yield the same result. Hence there is every reason to admit that the grafting of the organ of an ape on a man may be compared to a graft from man to man (homograft). New horizons thus open upon the future of grafting in general, and especially on that of the sex gland.

Hard though it be to obtain apes, it will always be a task less arduous than that of inducing young men to give up one of their glands. We might undertake to raise apes as we raise our domestic animals, the more so since they are extremely prolific.

The ape as the guardian of vital energy transmissible to man will be looked upon as a most valuable animal, which will unfailingly be accorded the most attentive care.

Men who have reached the age when their intellectual and physical faculties begin to decline, when the memory becomes unreliable, thought is slow, effort more difficult, fatigue more prompt, when all the ardors of life are blunted and dulled and some are extinguished,

may borrow from their young relatives of the virgin forests a new source of vital activity.

And women? When they reach the age where their powers betray them and decrepitude announces its presence, shall they be permitted to descend the fatal slope? Old age holds greater terrors for them than for us, and though they have less energy to expend during life, they aspire to preserve it none the less. The plastic surgery which we have practiced for many years and which, taken up again by some of our young and courageous colleagues, has recently been honored by the *Académie de Médicine,* has made such progress that it is easy for us to repair the outrages which the years have committed upon the faces of our friends. The only women who keep their wrinkles are those who are ignorant of the resources which surgery has placed at their disposal, or those who have lost the instinct to please.

To reconquer the face of twenty years ago while preserving the vital energy which, in the case of woman, shows itself in bodily supple-

ness and grace of movement, means that she has once more found the joy of living. But to take on the semblance of youth again and retain the body stiffened by sixty years of living, what irony!

I would not, however, advise women to undergo the graft of the male sex gland. Indubitably they would acquire new vigor; but, what they might gain as regards strength they would lose in grace.

In fact, after similar graftings on she-goats and on ewe-lambs, I have noticed a species of perversion of the maternal instinct, hence a change in their psychic state, in their affective sentiments. And the body might undergo changes no less unfavorable in the case of woman. Man's distinguishing signs—mustaches, beard, heavy voice—are also dependent on his sex gland, and these are all things which woman has no wish to acquire. Incidentally, woman has no need of borrowing from man something contrary to her nature. In her youth she gives evidence of such an exaltation of all her faculties, such a running

over of vital energy, that without doubt she possesses a gland of her own, analogous to man's gland. Is it to be found in the ovaries? I believe it is. As in the case of man, the ardors of life in woman correspond to the most intense period of her sexual life, and there is, assuredly, a direct connection between the functions of the ovaries and those of all the other organs.

In fact, the ovariotomy practiced upon young women, far from their menopause, diminishes their vitality, and slows up their nutritive exchanges—hence an adiposity always strongly marked—and it often troubles their psychic state of being. This change is less noticeable during the first years following the operation, because the organism benefits by the ovarian secretion which the tissues have stored up, yet in the long run the symptoms grow more marked, and a premature subsidence shows itself in all manifestations of intellectual and physical life. Yet this change is far from being as marked as that observed in the case of man after castration. Is this

due to the fact that the male sex gland secretes a liquid more active than the analogous female gland, or does woman receive the energy which she shows during youth from still other glands called upon to supplement the weakness of her ovarian secretions? It is difficult to answer this question. The study of the internal secretions of the ovaries has, in fact, not advanced very far. We have not as yet been able to determine whether this secretion is produced by the epithelial cells of the ovaries, or whether it is secreted by the *yellow bodies* which form in the ovaries after the bursting of the Graafian follicles and the expulsion of the ovules. New researches will therefore be necessary which will not delay bringing about a solution of the problem in which women have so great an interest.

The graft of a young ovary in full activity might, very probably, breathe into woman a new vital energy adapted to her constitution. In the meanwhile I can only offer this consolation: the mortality statistics of every land prove that women live much longer than men.

Hence they already have the advantage of us and consequently may still wait a few more years before the experiments in course of development bring them the remedy which is to intensify and prolong their existence.

As to men, I have every reason to hope that, from the present moment forward they may benefit by the new acquisitions of experimental science. The graft of the testicle will suffice in the majority of cases. In others, it will be necessary to add to it a graft of the thyroid gland as well. These two glands are, in fact, intimately united. The atrophy of one often entails the atrophy of the other. Both play a capital part in our organism, and while the sex gland augments the energy of the nobler cells of our body and supports them in their resistance against the invasion of the conjunctive cells, the thyroid gland abates, or to be precise, modifies the activity of these conjunctive cells and prevents them from multiplying too rapidly, to the detriment of our life.

Hence the thyroid gland is a precious auxiliary in the struggle which our specialized cells

maintain against the conjunctive cells, and, in view of this, its graft may at times be indicated. An attentive examination, a study of the symptoms by which the decline of each gland is betrayed, will serve as a guide to determine the line of action marked out in each case.

It is an additional sacrifice we must demand of the apes. As to man, the grafting of one or two glands remains one of the most favorable operations he may be called upon to undergo.

CHAPTER VII

The future of organic grafting—The grafting of bones, of skin, of the tendons, of the nerves, of the internal organs, and of the glands—Effect of the internal secretion of the sex gland on the intellectual faculties and the aptitude for work—The great services which may be rendered the community by aged persons, rich in acquired experience and accumulated knowledge, owing to the graft of the sex gland—The prolongation of life.

We have just studied the effect of the graft of the sex gland on the organism. Can this method be generalized? Can we make our body undergo the same treatment in an operating room to which we subject a machine in a repair-shop, when one of its parts has been rendered useless? Evidently the conditions are not the same in both cases. Not only do we not know how to construct the human machine, but we are not even capable of manufacturing the least one of its organs. In order

to replace them we are obliged to make use of the organs which nature has formed in bodies similar to our own. And therein lies the great difficulty. The advance actually realized by science allows us to replace an organ worn or destroyed by another, on condition, however, that we find the spare organ.

As regards the bones, the problem is simple enough. From primitive times we have retained a bone which was serviceable to us in climbing trees. Yet since we make but little use of this form of exercise, this bone is of only mediocre advantage to us. Hence it may be removed without any damage done to our walking or standing. Running animals, such as the horse and the dromedary, whose ancestors were also running animals, possess this bone only in an altogether rudimentary state. The bone in question is the fibula, found beside the tibia. The latter is sufficiently solid to be able to dispense with its neighbor's assistance.

When we have to repair a fracture of one of our bones—such cases were frequent during the war, and still occur often enough as a re-

Fig. 32

Louis R. Before the operation: the forearm is twisted outward. The wounded man is obliged to support it, the radius showing a loss of osseous substance.

Fig. 33

Louis R. Two months and a half after the operation. The forearm is straight. The wounded man executes any movement with ease.

sult of accidents or maladies—it is easy for us to borrow part of someone's fibula and fit it in between the two ends of the broken bone. We were fortunate enough to be able to give the wounded in our hospital, from the beginning of the month of October, 1914, the benefit of this method of bone-grafting, fathered by the great Lyons surgeon, Ollier (Figs. 32, 33).

We can also find the material for the graft on the patient himself, when it is a question of replacing a tendon which has been torn out. We possess tendons large enough to allow us to borrow from them, a loan which, incidentally, may also be obtained from the abdominal aponeurosis, that large and resistant membrane which doubles the muscular and cutaneous wall of the abdomen.

The skin may also be replaced without much difficulty, either by borrowing skin from a covered place in order to benefit a place exposed to view, as we had an opportunity of doing for a young girl whose face and hands had been horribly burned, by using for our grafting material the fœtal membranes which envelop the

child at birth (Figs. 34, 35). It is also easy enough to replace a section of artery in the case of aneurism, when the dilated coats of the vessel, forming a tumor, are ready to burst, which inevitably brings about the death of the patient. In this case one removes the arteries of a corpse immediately after death, and preserves them in a refrigerator ready for use at the proper moment.

The same procedure may be employed when we are confronted with the substitution of a destroyed articulation. Kuttener, on June 4, 1910, replaced the articulation of a knee attacked by tumor by an analogous articulation removed three hours after death from a patient in his hospital, and preserved for twenty-four hours on ice. The fact was established that on June 19, 1911, a year after the operation, the patient, who had been at home for six months, stood without support, walked without the aid of any mechanism, and carried out all the movements of flexion and extension with his borrowed knee. On December 18, 1915, we presented at the *Société de Biologie,*

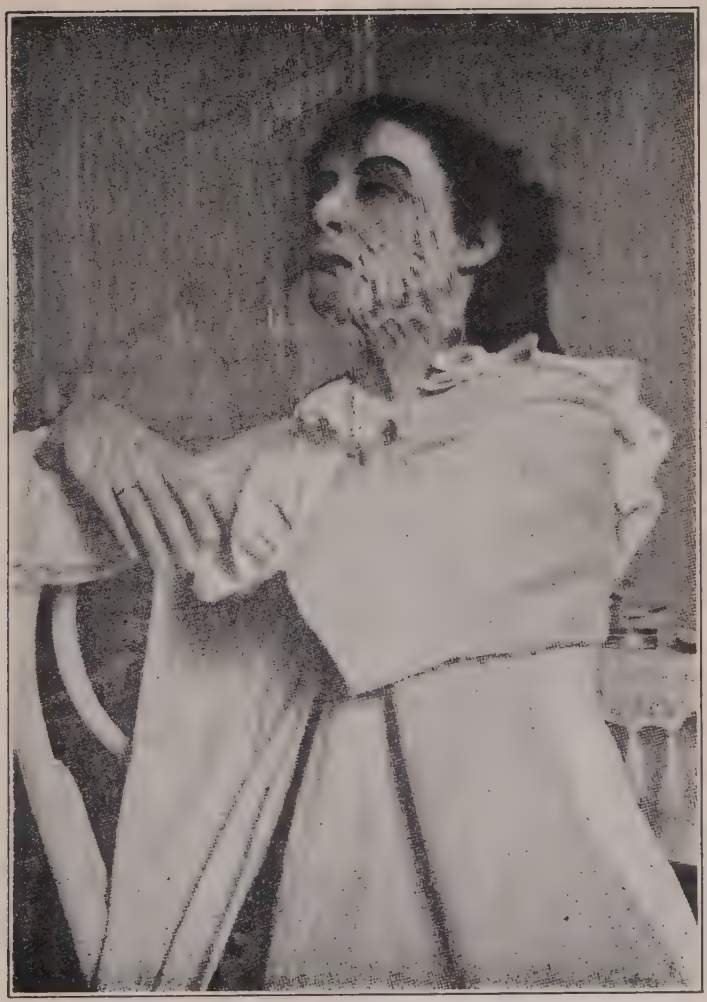

Fig. 34

Young girl with burned face and hands. Photograph taken the day before the operation.

Fig. 35
The same young girl a year after the graft of fœtal membranes.

FIG. 36

Dog, No. 12, fifteen months after operation. The graft was made on the metacarpophalangeal articulations of the left leg.

dogs walking with grafted articulations, fifteen months after the operation (Fig. 36).

Fragments of nerves may also be employed in the same manner to replace those which have been destroyed, and it is possible thus to cure muscular paralysis resulting from similar lesions.

The difficulties increase, however, though they are not insurmountable, when one attempts to graft an internal organ or a whole member. Thus it has been possible to graft ovaries upon women who were sterile, or who had been surgically deprived of these organs, by borrowing them from another woman in process of an operation necessitating the removal of the matrix. Even in this last case, no matter how useful the preservation of the ovaries might be for the maintenance of her vital energy, the woman could without disadvantages sacrifice one of them for another of her sex.

Morrice, at the beginning of the year 1895, thus obtained a good result, and the woman in whom he had transplanted the borrowed ova-

ries gave birth on March 15, 1906, to a girl weighing seven and a half pounds.

We have already recorded elsewhere the similar result which had obtained by grafting on an ewe-lamb, after having removed her own ovaries, the ovaries of another ewe of the same drop.

The grafting of kidneys has also been realized, but only on cats and dogs, by Carrel. It has not as yet been carried out in the case of man, and yet, in certain instances, only the grafting of this organ will save the patient. Thus it is possible to combat tuberculosis of one kidney by its removal; yet when the second is in turn removed, the substitution of another is the only thing to prevent the fatal issue. The kidney of a healthy man, killed by accident, and at once removed, might answer for this operation. Could that of one of the superior apes be employed in such a case? The future will tell us. Yet what may already be looked forward to is the grafting on men of their glands: these essential organs which command the functions of all our tissues.

Opotherapy, which consists in administering the glands of animals, when our own fail us, represents an excellent treatment, but a palliative one. In order to support the heart-beat, and the contractions of the blood-vessels, the suprarenal gland pours the necessary quantity of the precious liquid into the blood at every moment. All the glands act in the same manner; their functions are continuous and adjusted to our needs; while the absorption of glands, by no matter what form of medication, cannot help but be clumsy. Its effect, under these conditions, necessarily brutal, in no wise conforms to the slow and continual processes of nature.

Not long since opotherapy represented a notable step in advance in the treatment of a large number of our ailments, but at present we can do better. As we increase our knowledge of our own body and dare more, our field of action continues to extend. Surgery has attained its culminating point in the art of removing a large number of our organs, and in curing the malady from which we are suffer-

ing; but it deprives us of a function which formerly played a part in our constitution. The operation saves our life but curtails us bodily at the same time. The ideal toward which our efforts should tend is to replace that which has been taken from us, to return to our body the organ of which we have been deprived, since nothing in our organism is superfluous. One may live without a kidney, without a leg or an arm, yet one lives but poorly. The surgeon rejoices in the operation brilliantly performed, the patient exults because he has escaped death, yet the life of the individual suffers and is diminished as a result. Let us leave to the surgery of our fathers the part it has always played in delivering us from tumors, suppurations, etc., but for the new surgery born to-day, a far greater field of action opens. This surgery of the future lies in the grafting of our organs, our tissues and our glands. The path has already been blazed by the first pioneers. Despite all the tenacity of routine, all the difficulty the human spirit finds in liberating itself from the constraint of

reigning ideas, the new method will end by imposing its precepts.

We have a horror of decrepitude, of decay, of the infirmities of old age. Before we come to them each of us has tasted the joys which the expenditure of our energy has procured. We have learned to love work, and it has been pleasant for us to feel that we have been useful, that our efforts have contributed to the happiness of those near and dear to us, and to the success of some cherished idea.

And at that moment, when the experience we have acquired allows us to discern the mistakes we have made and recognize the deeds which time has justified, at that moment, when our spirit is ripe for the creation of great and beautiful works, our power to work abandons us. Memory weakens, thought lags, effort becomes painful.

We age too soon, we die before we are able to accomplish our task.

To restore to those men whose work has grown with their years, whose spirit is enriched by accumulated knowledge, whose soul

has been softened by contact with all the suffering experienced or witnessed during their long existence, to endow such men with new energy, and once more make them fit for productive labor, is to accomplish a work of social usefulness, to contribute to the world's progress.

Those who have seen in the grafting of the sex gland—which restores all energies —no more than the renewal of the source of those pleasures for which age has set a term, have only grasped a small side of the problem. The question concerns a higher and more universal domain. The graft of this gland will not merely contribute to the conservation and multiplication of the human race, and of those animals whose life we are interested in intensifying, but also to the duration of our intellectual powers and our ability to work. The ideal toward which our efforts tend is to preserve life in the plenitude of its diverse and multiple manifestations, to force death to retreat to its farthest limits.

May 10, 1920.

COMMUNICATIONS

BY

M. ED. RETTERER

Professor at the Faculty of Medicine of the University of Paris

TO THE

French Association for the Study of Cancer

AND TO THE

Biological Society

Translated by

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Extract from the Communication of M. Ed. Retterer to the French Association for the Study of Cancer.

Session of December 15, 1919

METAPLASIA

I should like to submit to you the results which I have obtained from various organs given to me by my friend Serge Voronoff. In order to study the influence which the testicles exert on the whole of the organism S. Voronoff has made experiments of testicular grafts on rams and goats, and at the Twenty-seventh Congress of Surgery he has presented the general results obtained by him. He has been kind enough to entrust to me the specimens of the grafted testicles for the study of the evolution of their tissues. In order to forestall misapprehension I add that these testicles have been fixed while fresh in picro-formol-acetic. After imbedding in paraffine I have made serial sections of from 5 to 7 μ which I have stained diversely. The preparations which I shall have the honor to submit to you will show you that I am able to make sections which are neither

oblique nor too thick, and that I can stain them in a precise manner. If I insist on these tedious details, it is because dissatisfied persons have been pleased to insinuate that my conclusions were founded on a defective technique.

Voronoff has grafted testicles even in the tunic of the scrotum. Although the blood circulation may be interrupted or suspended, the grafted tissue thus finds itself in its natural environment. Also the nutritive plasma goes to the superficial portions of the transplanted fragments, as well as to the cortical portions of the entire testicles. When these are young and still possess a thin albuginea, the cortical portions survive while the central ones die.

In the surviving parts nutrition is enfeebled. However, I have found even at the end of one year some seminiferous tubules with spermatids and heads of spermatozoa. The grafted testicle came from a young goat which had not yet formed spermatozoa. Consequently the spermatozoa have developed in the grafted tissue.

Figure 37 represents at a high magnification the structure of a portion of the testicle of the goat, taken a year after the graft. At 1, 1, there are fibrous trabeculæ containing cells with elongated nuclei and simulating smooth muscle fibers. At 2, 2, there are masses formed by nuclei joined by a common protoplasm. They resemble blind follicles of the epithelial stage, but the epithelial cells have a clear and poorly defined protoplasm. At their periphery they pass with-

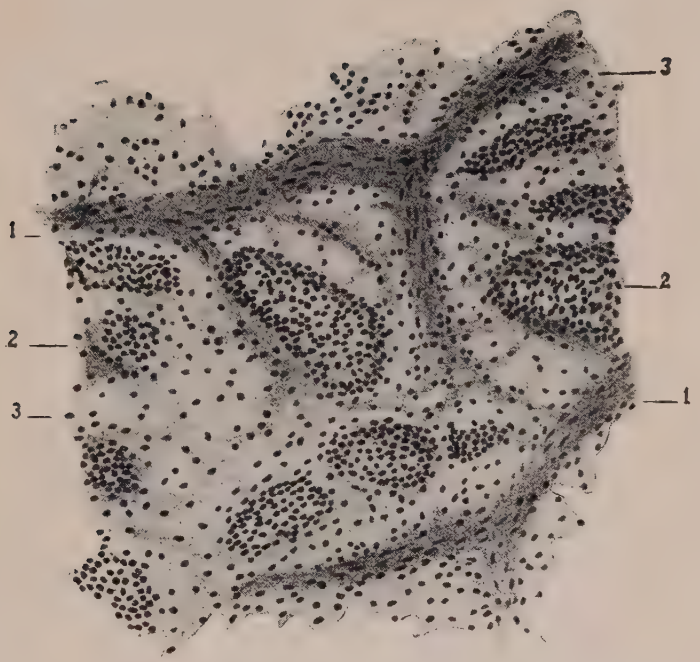

FIG. 37

Portion of a grafted testicle; one year after the graft. (Ocul. 1; obj. 7. Stiassnie.) 1, 1, fibrous strands; 2, 2, remnants of seminiferous tubules (blind follicles); 3, 3, reticulated tissue showing empty spaces.

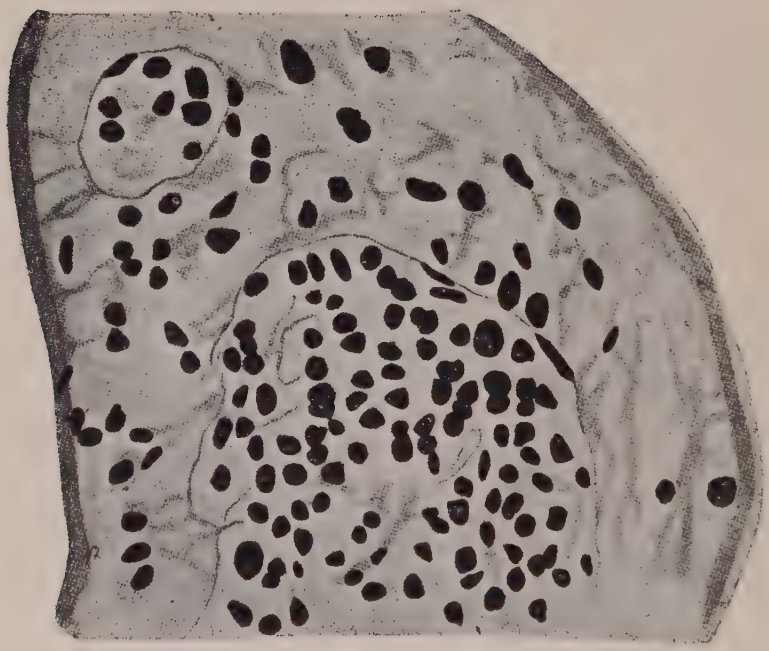

Fig. 38

Two blind follicles of Figure 1 with the intervening reticulated tissue. (Ocul. 6; immersion obj. 1/15e Stiassnie.)

out trace of a basement membrane into a reticulated tissue in which a number of free elements are present as a result of the dissolution of a part of the protoplasm. Comparing the grafted tissue with the testicles which had been grafted, and especially with grafted tissue obtained two or three months after the graft, it is easy to understand the evolution of the grafted tissue. In the normal testicle the tubules .10 to .12 mm. in diameter are contiguous and attached to each other and only at the hilus is there present a small amount of interstitial connective tissue. After the graft the interstitial connective tissue and that which constitutes the basement membrane develop into fibrous strands (1). As regards the seminiferous tubule, its outer epithelial cells are transformed into a reticulated tissue forming an envelope for the remaining central portion of the tubule. The latter exhibits the structure of an epithelial syncytium and simulates in the section a blind follicle at an early stage.

Figure 38 represents at a higher magnification two remnants of epithelial tubules with the intervening reticulated tissue. Between the reticulated tissue containing faintly staining threads and the epithelial remnant, there are hematoxylinophilic filaments which seem to penetrate into the epithelial remains. The cells of the latter themselves have a clear cytoplasm in process of dissolution. However, in several places may be seen granular and hematoxylinophilic filaments.

Figure 39 represents a portion of testicle two

months after the graft. Two seminiferous tubules, one in transverse and the other in oblique section, occupy the center of a mass picturing roughly a *blind* follicle. The epithelium of the tubules corresponds to the central layers of a normal tubule. The nuclei are large and have the structure of epithelial cells; the cytoplasm is clear and the cellular boundaries are effaced. The border of these epithelial remnants and of the sheath which encloses them is more sharply defined, especially at the lower portion of the left tubule, and at the entire periphery of the right one. The large nuclei of the epithelial remnant are followed by smaller and denser chromatic nuclei contained in a denser and better staining cytoplasm. As one passes from the epithelial remnant into the surrounding tissue, the cytoplasm differentiates more and more into a hematoxylinophilic reticulum and a hyaloplasm.

Figure 3 represents a stage intermediate between the epithelium and the reticulated epithelium containing empty spaces. I have described and pictured similar stages in the tonsils. The cells of the tubules or epithelial buds become enlarged, then little by little develop into a tissue of small cells in such a manner that several tubules give birth to an ovoid mass or blind follicle.

One might desire to explain the last picture by saying that the interstitial connective tissue proliferates and gives rise to a young tissue which strangles and chokes the epithelium of the semi-

Fig. 39

Portion of goat's testicle, two months after the graft. (Ocul. 2; obj. 7 Stiassnie.) Two seminiferous tubules, each surrounded by a shell of reticulated tissue whose spaces are filled with hyaloplasm.

niferous tubules. This hypothesis is unfounded, since neither I nor previous workers have been able to observe a single mitotic figure in the interstitial connective tissue. If the connective tissue increases at the same time that the seminiferous tubule diminishes in caliber, it can only be due to the transformation of the epithelial layers into a connective tissue which at first is reticulated, and later fibrous.

Hence as in the development of the tonsils, Peyer's patches and the pouch of Fabricius, we witness the formation of blind follicles. Several groups of epithelial tubules, comprising from six to eight ducts, form ovoid masses .3 to .5 mm., which at first consist of epithelial cords, and which finally form but a mass of reticulated tissue.

As a result of the graft, the epithelial elements of the seminiferous tubules, poorly nourished, change their structure and evolutionary cycle. Instead of producing spermatozoa, the greater part becomes transformed into reticulated tissue which represents the second stage in the evolution of the epithelial element. When the testicle finds itself placed under conditions where it no longer forms spermatozoa, the surviving epithelium evolves in another direction and produces different elements. Its evolution as an external gland thus suppressed, it continues to furnish elements for internal secretion. In the digestive tube we witness a similar division of labor in the parts which serve only as passage ways (pharynx,

pouch of Fabricius) or in which food does not remain long (appendix). The epithelial invaginations or open glands become transformed into blind follicles.

To sum up, the surviving portions of the grafted testicle may undergo an evolution which I might call regressive. The epithelial cells, poorly nourished, acquire a clear cytoplasm and divide into small elements which constitute a reticulated tissue. The dissolution of a part of the cytoplasm transforms the testicular tissue into an empty meshed mass or lymphoid tissue. *That which demonstrates the reality of the dissolution and resorption of the testicular plasma, is the fact that the presence of the grafted testicle assures to the subject all the secondary sexual characters (impetuosity of the male).*

Communication of M. Ed. Retterer to the Biological Society

Session of October 18, 1919

THE DEVELOPMENT OF TESTICULAR GRAFTS IN THE GOAT

At the Twenty-eighth Congress of Surgery, M. S. Voronoff presented the general results which he had obtained regarding the influence which the grafted testicles exert on the organism as a whole. As far as it concerns the evolution of the grafted

tissues, here is what I have observed in the specimens which M. Voronoff has entrusted to me.

I. *Testicles of very young goats which have been used as grafts.*—The testicles are still in a prespermatogenic stage with tubules .10 to .12 mm., lined by several layers of epithelial cells without spermatids or spermatozoa. The interstitial connective tissue has an extent of but 2 to 5 μ in the region of the hilus, and where the tubules touch each other there is only a thin membrane of 1 or 2 μ in thickness. Very rare are the ovid or polyhedral cells with abundant cytoplasm and fatty granules which are known as the *interstitial* cells. They are always isolated.

II. *Fragments of testicle grafted in the vaginal tunic of a castrated goat, 18 days after grafting* (No. 47).—The seminiferous tubules have a mean caliber of .10 mm. The interstitial connective tissue occupies an extent equal to that of the tubules. The greater part of the tubules have still a lining similar to that described above, but several show spermatids and heads of spermatozoa in shape of ovid mallets.

III. *Entire testicle grafted under the same condition, 12 days after the graft* (No. 49).—Necrosis of the epithelial cells.

IV. *Entire testicle grafted under the same condition, two months after the graft* (No. 60-B).—Necrosis of the epithelial cells.

V. *Fragments of testicles grafted under the same condition, two months after the graft* (No. 60-A).—In the sections of the fragments

may be observed three zones of tissue. The most superficial zone is connective in nature; the middle is reticulated and contains blind follicles; the third or deep zone is composed of seminiferous ducts about .03 to .05 mm. in diameter. At the boundary of the two latter zones one may observe the manner in which epithelial cells become transformed into reticulated tissue and blind follicles. Actually, groups of seminiferous tubules comprising two to ten ducts form ovoid masses of .3 to .5 mm. and constitute a blind follicle. In these follicles the epithelial cells of the tubules are multiplying, and though the cytoplasm still possesses the same staining properties as epithelium, it is strongly reticulated and in process of transformation into connective tissue. In other places the epithelial tubules do not group themselves into follicles, but from the periphery, toward the center the epithelial cells arrange themselves in concentric layers of very chromatic nuclei, while the cytoplasm becomes reticulated. The reticular tissue is destitute of interstitial cells.

VI. *Entire testicle grafted in the vaginal tunic of a castrated goat, 12 months after the graft* (No. 15).—Testicle of a very young goat, 15 mm. long and 5 to 7 mm. in width. The testicle had a thick albuginea of .15 mm. The testicle consists of a series of cords joined to each other by a reticulated connective tissue. The cords, cut transversely, are these rounded or ovoid masses the majority of which have a diameter of .05 mm., but there are some which attain a thickness of .1

to .2 mm. They consist of a common cytoplasm strewn with numerous small and very chromatic nuclei. Their periphery passes, without a basement membrane, directly into the reticulated connective tissue which at certain places is more abundant than the included cords, but which in general occupies only half the extent of the sum-total of cords. Cut transversely these form masses of .04 to .05 mm. composed of a common cytoplasm containing dense and very chromatic nuclei of 5 to 6 μ. Other cords .02 to .01 mm. in diameter have a center of the same structure, while their cortex consists of two or three concentric layers formed by similar nuclei but containing a more abundant and fibrillated intercellular substance.

The tissue which joins these follicular masses is plainly connective in nature with poorly staining nuclei. Interstitial cells are absent.

VII. *Graft of an entire testicle of a four months' old goat, three months after the graft* (No. 61).—This testicle 40 mm. long and 30 mm. wide, was enclosed in an albuginea 3 mm. thick. At the end of three months all the elements are in process of necrosis. The cytoplasm is granular and nuclei are absent.

Results and critique.—What becomes of the tissues of the grafted testicle? In Batrachians, Mantegazza (1860), Herlitza (1900), Solachas (1907); in Birds, Berchthold (1849), R. Wagner (1851), Lode (1895), Pézard (1918) have observed that the seminiferous tubules of the graft con-

tinue for some time to form spermatozoa, but little by little the epithelium degenerates, while there develops between them a plastic exudate, then a fibrous or connective tissue which does not have the structure of the classic interstitial tissue. The testicle of mammals, when transplanted into the peritoneal cavity or underneath the skin, shows at the end of a certain time only the cells of Sertoli which multiply by mitosis and become converted either into giant cells or into an indifferent epithelium (Ribbert, 1898; Maximow, 1899; Cevolotto, 1909). In 1909 Steinbach grafted the testicles of 46 young rats on the internal surface of the abdominal wall. The majority of the grafts survived. The seminal cells degenerated and the seminiferous tubules became lined by only a "succulent" epithelium. The interstitial cells became more abundant. *Quite different from his predecessors, S. Voronoff has grafted the testicles even in the tunic of the scrotum.* Although the blood circulation may be interrupted and suspended, the graft finds itself thus placed in its natural environment. Also the nutritive plasma reaches the superficial portions of the transplanted fragments, as well as the cortical portions of the entire testicle, when these have only a thin albuginea. All of the portions supplied by the plasma survive, the central portions alone die.

In the grafts which survive the nutrition is weakened. They show, however, some tubules whose epithelial cells differentiate and produce

heads of spermatozoa. The majority of the other seminiferous tubules likewise survive. But the developmental processes are retarded at the same time that the epithelial cells become changed into a syncytium containing numerous nuclei, which fills the lumen of the tubule. The syncytium is then transformed, starting from the basement membrane, into a reticulated tissue, i.e., the cytoplasm differentiates into a hematoxylinophilic reticulum and a hyaloplasm. As the hyaloplasm subsequently undergoes dissolution, the reticulated tissue at first filled, shows empty spaces. Thanks to this process the interseminiferous connective tissue becomes more abundant. I have never seen any mitotic figures in the interstitial tissue, hence it is not the proliferation of the connective tissue cells which augments the mass of interstitial tissue.

As a result of the graft, the epithelial elements of the seminiferous tubules, poorly nourished, thus change their structure and evolutionary cycle. Instead of producing spermatozoa, the majority becomes transformed into reticulated tissues, which represents their second phase of evolution. In the grafted testicle the epithelium assumes at first such form and structure which we find in the anlagas of the pouch of Fabricius, the tonsils, Peyer's patches, etc., namely an epithelial lining analogous to that of open glands. But little by little this epithelium becomes transformed into reticulated tissue. Experimentally, I have succeeded in inciting the formation of fi-

brous nodules at the expense of epithelial buds. The testicular graft realizes the conditions which are favorable to the transformation of glandular epithelium into reticulated tissue.[1]

Conclusion.—In the grafted testicle (entire or part) there survive only the superficial portions which continue to receive the nutritive plasma. But the epithelial cells which survive modify their structure and their evolution. Very few continue to divide in order to produce small nuclei and heads of spermatozoa. The majority, under these new conditions, become transformed into a syncytial mass which finally develops into reticulated connective tissue.

Communication of M. Ed. Retterer to the Biological Society

SESSION OF OCTOBER 25, 1919

THE EVOLUTION OF TESTICULAR GRAFTS IN THE RAM

The testicular grafts which M. S. Voronoff has practiced on the ram have been made partly under similar conditions as those of the goat, and partly under different conditions. Their histological study has given me the following results.

[1] This, so to speak, internal evolution of epithelium is especially accentuated in those portions of the digestive tube, which serve only for passage or where the chemical activity is greatly reduced (pharynx, *touxille colique*, cloaca of birds, etc.). (Retterer et Lelièvre, 1910.)

I. *Testicle of a young ram which had been used as a graft.*—The seminiferous tubules have a caliber of .15 mm. They are attached to each other, and for the greater part of their circumference are separated only by a lamellated membrane of 3 to 4 μ. At the hilus the connective tissue is more abundant, but interstitial cells are rare. Each tubule is lined by four or five layers of epithelial cells forming a wall of .04 mm., and enclosing a lumen of .07 mm. filled with cellular detritus. The majority of the cells which rest on the basement membrane have a very chromatic nucleus, and only few clear nuclei containing a nucleolus are seen. The cells of the middle layers have a transparent cytoplasm of 15 to 18 μ with a nucleus of 7 μ mean diameter. They are separated from each other by a sharply defined membrane. The cells which border on the lumen are smaller and in process of disintegration.

II. *Graft of an entire testicle* (No. 70).—A year after the graft the testicle has the following structure. Instead of the seminiferous tubules there are seen only epithelial cords whose caliber varies between .035 and .040 mm. The cords are separated by connective tissue strands .02 mm to .05 mm thick. Instead of the basement membrane formed by a connective tissue strand there is a layer 7 μ thick composed of a cytoplasm which is granular and stains red with eosin and orange, like the epithelium of the cords. The nuclei contained in this peripheral layer are placed far apart. The epithelial cord itself consists of the

following elements: (1) one or two layers of peripheral nuclei, (2) a central mass. The peripheral nuclei 4 to 5 μ in diameter are rounded and very chromatic. The internuclear cytoplasm is scanty, does not exceed 1 or 2 μ in thickness. The central portion is 60 to 70 μ thick and comprises a mass of cytoplasm containing few nuclei.

III. *Fragments of testicles grafted on the vaginal tunic of an old ram whose own testicles remained in place. Grafts taken* 14 *months after the operation.*—The seminiferous cords have a caliber of .06 mm. to .10 mm. The interstitial connective tissue has an average thickness of .05 mm. The seminiferous cords, the majority of which no more possess a central lumen, have a varying structure according to the region. At the periphery of the grafted fragments the center and the middle layers are occupied by small nuclei and flattened ovoid filaments having all the structural and staining properties of spermatozoa. Other cords contain large polyhedrous epithelial cells each provided with a nucleus. Others again have the structure of bands of reticulated connective tissue in the center of which persist epithelial cell masses. In the central portions of the grafted fragments, the seminiferous tubules contain cytoplasmic masses in process of degeneration with few or no nuclei.

As in the goat, the reticulated tissue develops in the ram at the expense of the epithelial cells of the seminiferous tubules. These differentiate, beginning with the external layers, into a retic-

ulum and a hyaloplasm. The latter has a varying fortune. In certain places it undergoes dissolution and there remains only a reticular tissue with empty meshes. In other places it forms connective tissue fibrils, and the testicular tissue becomes transformed into a fibrous mass.

Results and critique.—Though used under conditions very little different from the goat, the testicular grafts of the ram develop as in the goat. The epithelium continues at certain places to develop small nuclei and heads of spermatozoa. But for the larger part it becomes transformed into reticulated tissue. With this developmental deviation is connected the question of the influence which the grafted tissue exerts on the other tissues of the organism. In the old ram (No. 12), enfeebled, fearful and showing a total extinction of generative ardor and of the "potentia coeundi," the grafted tissue has caused the rebirth of the "libido coeundi" and the virile impetuosity of the male. Placed together with a ewe, he has covered and fecundated her, and the ewe has thrown a vigorous lamb.

Which are the elements of the grafted testicle which modify the general behavior and give to the bearer the virile characters (vigor, *libido* and *potentia coeundi*). It is said that the cyptorchids present largely analogous manifestations. They are likewise observed after ligation of the vasa deferentes and the action of X-rays. Since under the last named conditions the interseminiferous connective tissue becomes more abundant and

richer in interstitial cells, the latter have been regarded as forming a secretion which is absorbed and acts on the entire organism (*internal* secretion). In the grafted tissue cellular division in the interseminiferous tissue is absent. Hence its hypertrophy is not due to the proliferation of the connective tissue cells. Besides, observers have never seen any mitotic figures in the interstitial cells or in the cells of the connective tissue. The interstitial connective tissue becomes more abundant because the epithelium of the seminiferous tubules becomes transformed into reticular tissue. As regards the *interstitial* cells, they are thinly scattered and very rare in the normal goat and ram. It is the connective tissue cells which become filled with fat in animals which are being fattened. In the grafted testicles I have not been able to observe this. Consequently it is not the interstitial cells which here take charge of the internal secretion.[1]

Others (Loisel, Champy, Pézard) maintain that in the birds and the batrachians the cells of Sertoli fulfill this rôle. In the grafted testicles

[1] It is well to recall some of the conditions under which the interstitial cells appear or disappear. In the moles these cells are abundant before rutting time. During the rut they are scanty, after the rut, their number increases. During hibernation they disappear. In the batrachians and birds the interstitial tissue is well developed before puberty, but becomes reduced with the beginning of sexual activity.

All these facts agree with those which we have observed in the goat and ram. The *libido* and *potentia cœundi*, far from occurring in direct ratio with the number of interstitial cells (cells filled with fat), coincide with the diminution or disappearance of these elements. Besides, it is an old saying that a cock grown fat is not a good cock.

there no longer exist either the cells of Sertoli or the spermatogenic cells. The whole epithelium of the seminiferous cords forms a syncytial mass which at first shows a reticulum whose meshes are filled with hyaloplasm, and finally one with empty meshes.

In summing up the evolutionary phenomena observed in the grafted tissues we will say that the interseminiferous tissue becomes more abundant in proportion as the seminiferous cords diminish. Simultaneously, the epithelium of the cords becomes transformed into reticular tissue whose meshes are filled with hyaloplasm. Then the hyaloplasm liquefies and becomes absorbed, hence the reticulum with empty meshes. It is to the production and resorption of this plasma, formed by the originally epithelial testicular cells, that we must attribute, in our opinion, the influence exerted by the testicle on the other tissues of the organism. In the testicle, as in the liver and pancreas, the agent of external and internal secretion is the epithelial cell which is at once *exocrine* and *endocrine*. In the grafted testicle the epithelial cell becomes changed and functions only in an endocrine capacity.

Conclusion.—The epithelial cells of the seminiferous tubules lose during their transformation into reticular tissue, a plasma whose resorption determines the secondary sexual characters.

Communication of M. Ed. Retterer to the Biological Society

SESSION OF NOVEMBER 8, 1919

TESTICLES OF THE AGED

The evolution of testicular grafts has definitely demonstrated to me several facts which I had surmised from a study of the testicle of the aged. I have, therefore, undertaken again the study of the latter and following are the results which I obtained from old men of sixty-eight and seventy-four years.

The testicular substance of the aged is soft. For fixing and hardening I have used a mixture of formol and Müller's fluid. The epithelial elements of the seminiferous tubules are, as we shall see very brittle, hence to obtain sections without any air spaces, it is necessary after the paraffin impregnation to cut thick section of 15 to 20 μ.

The greater part of the old testicles is not formed by tubules but by epithelial cords. In numerous places, though of comparatively small extent, these cords with the exception of their internal layer have undergone transformation into fibrous connective tissue.

The epithelial cords have a caliber of .12 mm. to .15 mm. They are separated from each other by septa of fibrillar connective tissue with abundant cells and mallet-shaped nuclei. The septa

are continuous from one tubule to another with blood vessels placed centrally. They contain interstitial cells filled as is shown by Sudan III, with a mass of fatty granules. I have not been able to distinguish a true basement membrane between the septa and the epithelial lining. This latter practically fills the whole cord, for the central lumen is indicated only by a very narrow cleft or perhaps by a transparent cytoplasmic layer beneath the nuclei. The epithelial lining is .03 mm. to .05 mm. thick, and consists of 5 or 6 layers of nucleated cells. The nucleus of these cells are rounded. In the external layers it measures 5 μ in the middle it is 5 to 6 μ in the internal layers finally it attains a size of 7 to 8 μ. In other words, the cells and especially their nuclei increase in size from the periphery to the center of the cord. The cytoplasm of these epithelial cells is formed of granular filaments arranged in such a manner as to constitute a dense reticulum whose narrow meshes are very poor in hyaloplasm. The granular reticulum stains with hematoxylin, and the hyaloplasm with acid fuchsine.

As regards the regions which seemingly consist only of fibrous tissue, and which we shall call *vesiculo-fibrous islets,* they likewise possess cords but these are greatly reduced in size and have an entirely different structure. There are in fact some cords .02, .03 or .04 mm. which are lined by only one layer of cylindrical cells and containing a central slit; others showing 2 or 3 layers of

epithelial cells; and finally some, especially at the periphery of the islets, which show all stages of transition between the last named cords and the epithelial cords described above. Between the cords (of the islets) there is found a dense connective tissue whose fibrils are concentrically disposed around the cords. The cells of this tissue are characterized by the following structure. The nucleus is surrounded by a zone of clear cytoplasm of 3 to 4 μ, while the peripheral zone is granular and reticulated. The same vesicular cells are found in the epithelial lining of the reduced cords of the fibro-vesicular islets.

These vesiculo-fibrous islets develop as follows: In the regions where there are still cords with several layers of epithelical cells, certain cords show in their external layers, nuclei surrounded by a clear perinuclear zone and a peripheral zone which is becoming fibrillar. In proportion as this transformation continues from the periphery to the center of the cord the vesiculo-fibrous septum thickens and the epithelium is reduced to a double or single layer. When this process extends over a large number of cords, there is formed a vesiculo-fibrous islet whose cells recall the structure of the vesicular nodules of supporting tissue, as for instance the sessamoid of the tendon of Achilles of the frog.

To sum up, in the testicle of the aged the epithelium of the seminiferous tubules continues to multiply, producing cellular layers with large nuclei. Not only does this lining persist to trans-

form the tubules into cords, but the epithelial cells become vesicular and change, progressing from the periphery toward the center, into vesiculo-fibrous tissue.

Results and critique.—According to Bichat, Cruveilhier, etc., the testicle becomes soft and shriveled in old age. According to others, Arthaud, Coyne, Riess, etc., the perivascular and pericanalicular connective tissue becomes hypertropied, strangles and chokes the epithelial tubules which degenerate. Thus the testicle becomes indurated. Still others maintain that the tubules become transformed into epithelial cords, and agree with Benda, that the testicle returns to a state similar to that of early youth, as though the decline of age were in reality a rejuvenation. The existence of cords, rather than tubules, explains the failure of Follin who was not able to inject the testicular tubules of old persons. But certain tubules continue to produce spermatozoa, since Duplay, and later Dieu, has found them in the seminal vesicles, in 68 out of 100 sexagenarians, 59 out of 100 septagenarians, and 48 out of 100 nonagenarians. Desnos[1] has seen them even in the seminiferous tubules of old persons. He has moreover described the thickening of the basement membrane as well as of the epithelial cells of which the outer are granular and polygonal, the middle granular and spherical, and the inner granular and having numerous processes.

[1] Annales des organes génito-urinaire, 1886, p. 72.

J. Griffiths[1] attributes all the facts which he had observed in the old testicles to degeneration and chronic inflammation. The single layer of tall or columnar cells which he had seen in the reduced tubules corresponded to the external layer, while the more internal layers were undergoing fatty degeneration. The intertubular tissue thickens and the basement membrane likewise hypertrophies. Griffiths did not say what process effects this increase in thickness. However, he expressly notes that the fibrils of the basement membrane are continuous with the fibrils of the columnar cells. This fact proves, in my opinion, that the basement membrane is due to the transformation of the epithelial cells into connective tissue elements.

Griffiths has well described and pictured the clear zone which encircles the nucleus of the epithelial cells lining the tubules of the fibrous islets. But he did not understand its significance. Many years ago I have shown[2] that in the connective and epithelial tissues the cells which are in nutritive superactivity or in process of transformation into a different type of cell, acquire a clear cytoplasm around the nucleus (vesicular cells). Hence I can not accept the opinion of Griffiths who concludes that these epithelial cells degenerate. It is true that he admits the persistence of the most external layer whose elements

[1] Journal of Anatomy and Physiology, t. xxvii, p. 474, 1893.
[2] Comptes rendus de la Soc. de Biologie, 1916, p. 1117, et ibid., October 12, 1918, p. 829.

assume a columnar shape. In my opinion it is the central layer which undergoes these morphological changes, while the more external layers become transformed into fibrous tissue in which the vesicular cells persist (fibro-vesicular tissue).

With the progress of age the epithelial cells of the testicle become enriched with hematoxylinophilic filaments, and the hyaloplasm contained in the meshes of the reticulum becomes firm and no more undergoes dissolution. These cells do not degenerate. The most internal ones grow to form a very tall layer, while the middle and external ones develop so as to produce fascicles of connective tissue. At the same time the nuclei of these various layers surround themselves with a clear cytoplasm (vesicular cells). Far from considering these cellular phenomena as signs of degeneration, I see in them the manifestations of a progressive evolution. It is true that the testicular epithelium forms but few spermatozoa. But it is actively alive, for it produces epithelial layers the greater part of which develop into fibrous tissue.

Conclusion.—With the progress of age, the epithelium of most seminiferous tubules, instead of forming free elements, builds up numerous cellular layers which persist and the greater part of which develops into vesiculo-fibrous tissue.

Communication of M. Ed. Retterer to the Biological Society

SESSION OF NOVEMBER 15, 1919

CONDITIONS WHICH CAUSE VARIATION IN THE DEVELOPMENT OF THE TESTICULAR EPITHELIUM

Besides the grafted testicles and the testicles of the aged, I have studied the epithelium of the seminiferous tubules in young adults and in an ectopic testicle.

I. *Testicles of two subjects (twenty-five and thirty years) killed.*—Fixation while fresh in picro-formol-acetic. The seminiferous tubules have a caliber which varies between .12 mm. and .15 mm. The parietal cells of the tubules (spermatogones) not only have a large nucleus (9 to 12 μ), but their cytoplasm is granular, i.e., formed by a dense reticulum of hematoxylinophilic filaments. The following layers (spermatocytes) show a slightly smaller nucleus, a clear cytoplasm surrounding the nucleus and a cortical cytoplasm granular like that of the spermatogones. Approaching the inner layers the granular cytoplasm is reduced to delicate anastomosing trabeculae. Finally there are seen the masses of elements with small nuclei (spermatids), very chromatic and measuring each only 2.5 μ or 3 μ. They are

found in the wide meshes bounded by the granular filaments, and are still surrounded by a very clear cytoplasm. During their transformation into spermatozoa, the spermatids remain embedded in a fluid cytoplasm which undergoes dissolution and sets the former free.

Thus in its evolution, starting from the periphery of the tubule, the replete and densely granular cytoplasm acquires a clear hyaloplasm which accumulates between the granular anastomising strands. The hyaloplasm contained in the network formed by the latter becomes pitted with vacuoles around the spermatids and spermatozoa which have developed at the expense of the nuclei and the perinuclear protoplasm. The vacuoles fuse and liquefy, thus setting free the spermatozoa. But these continue to form distinct masses on account of the hematoxylinophilic septa which project from the reticulum of the testicular cells. Thus the epithelium of the outer layers of the seminiferous tubules becomes composed of a densely reticulated protoplasm. In the middle layers the meshes enlarge and the hyaloplasm which fills them becomes more and more abundant. Finally in the central layers the hyaloplasm liquefies and sets free the spermatids and the spermatozoa.

II. *Ectopic testicle of an adult.*—The consistency and general aspect of this testicle would place it in the class of fibrous testicles of the anatomo-pathologist. The albuginea whose thickness varies between .4 mm. and .5 mm. is continu-

ous at numerous places with a layer of about 1 mm. whose fabric, likewise fibrous, seems pitted with narrow irregular slits. Toward the center these slits are continuous with ducts, .10 to .15 mm. in diameter, which have no lumen, being completely filled. Instead of having an ordinary epithelium they have quite a different structure, namely a reticulum of slender filaments, very hematoxylinophilic, whose wide meshes are filled with a transparent cytoplasm.

The tubules or ducts of the central portion are surrounded by a basement membrance and filled with epithelial cells disposed in 1, 2 or 3 rows. It almost reminds one of the reticulated epithelium of the enamel organ. Approaching the middle layer which separates the central portion from the albuginea, the peripheral epithelial cells are seen to assume the characters of connective tissue cells which are continuous with the fibrous fabric without the interposition of a basement membrane.

The ectopic testis recalls the vesiculo-fibrous islets which characterize the testicle of the aged. The epithelium of the central tubules is in process of transformation into reticular tissue. In the middle layer the recticulated tissue with filled meshes undergoes a fibrous evolution, i.e., the hyaloplasm produces connective tissue fibrils.

To sum up, in the testicle of the adult in sexual power, the granular and hematoxylinophilic cytoplasm of the external layers differentiates in the middle layer into a peripheral reticulum and

an abundant perinuclear hyaloplasm. This latter becomes more and more liquid in the central layers, and finally liquefies completely, thus setting free the spermatozoa. On the contrary, in the ectopic testicle, as in that of the old, the hyaloplasm of the testicular tubules becomes denser. Instead of disappearing by liquefaction, it produces connective tissue fibrils, which transform the organ into a fibrous mass. In the normal adult the epithelial cell of the testicle is characterized by the production of an abundant hyaloplasm which ultimately liquefies. In the old or ectopic testicle the hyaloplasm becomes denser, hardens and produces connective tissue fibrils.

General Results.—In the embryo, fœtus and infant, the epithelium of the testis is arranged in the form of cords, .05 to .06 mm. wide, in the center of which there appear gradually empty spaces due to the dissolution of the protoplasm. Already at this period we distinguish in the midst of the syncytium composed of granular, poorly delimited cells, large cells whose perinuclear cytoplasm is clear (spermatocytes). These spermatocytes become numerous towards puberty and their nucleus 10 to 12 μ divides giving rise to cells with a progressively clearer cytoplasm. The spermatocytes continue to multiply, each giving rise by dividing twice to four little cells (spermatids) whose nucleus is one-fourth the size of that of the original cell. In order to set free the spermatids, the clear cytoplasm undergoes dissolution and there only remain some hema-

toxylinophilic filaments partitioning the lumen of the seminiferous tubule. The mitoses responsible for the proliferation of the testicular epithelium are accompanied by the formation of an abundant protoplasm which in conjunction with the production of the cellular elements, contributes to the increase in caliber of the seminiferous tubules.

With age, the division of the germinal epithelium become less frequent. The cells become more granular in structure. The cytoplasm undergoes but a very limited dissolution. The epithelial cells arrange themselves in several layers and the lumen is reduced to a very narrow slit which is at times filled up by a protoplasmic layer. In this manner the seminiferous tubule changes anew into an almost solid cord. The central cells divide less and less into small elements, the spermatids and spermatozoa become less and less frequent. However, the testicular epithelium is living and continues to evolve, though in a different way than that of the adult in sexual power. The epithelial elements become enriched with hematoxylinophilic filaments and a dense hyaloplasm, and beginning at the external layer the hyaloplasm produces connective tissue fibrils. In this way the epithelial cords diminish in caliber, the intercordal connective tissue increases and the testicle is partially transformed into islets of fibrous tissue containing cells with clear perinuclear cytoplasm, similar to those seen in epithelial cells which are in process of transformation into connective tissue.

In the ectopic testicle of the adult the testicular epithelium shows an evolution analagous to that of the old testicle. Arthaud has noted this fact in 1883, and has studied it with Monod in 1887. The connective tissue thickens and hardens around the blood vessels and seminiferous tubules in both the ectopic and the old testicle.

Felizet and Branca[1] have described and pictured (ectopic testicles of 9- and 13-year-old infants) a connective tissue frame-work very extended and highly developed, and containing infrequent epithelial tubules in a rudimentary state. This would be the primitive morbid condition of the ectopic testicle. But the text is silent on the following point: What is the process which causes hypertrophy of the connective tissue and atrophy of the epithelium?

In the testicular grafts the epithelial cells change for the most part into reticular elements whose meshes at first filled with hyaloplasm soon become empty. Instead of becoming at once fibrous tissue, the epithelium passes through a reticular stage. The ultimate dissolution of the hyaloplasm produces, in my opinion, the plasma whose resorption determines the *libido* and the *potentia coeundi* of the subject bearing the grafted tissue (previously castrated). In the cryptorchids and the aged the epithelial cells change directly into fibrous tissue, and there is formed no hyaloplasm which dissolves and is

[1] Journal de l'Anatomie, 1898, 1899, p. 205 and p. 329.

absorbed. Thus the fibrous transformation leads to the same results as castration, since in either case both the external and internal secretion is suppressed.

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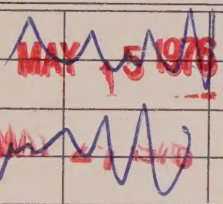

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